

Block copolymers as sequestering phases in two-phase biotransformations: effect of constituent homopolymer properties on solute affinity

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Abstract

BACKGROUND: Block copolymers can be effective extractants in solid–liquid two-phase partitioning bioreactors (TPPBs) when selected on the basis of their partition coefficient toward target solutes, and their thermo-mechanical properties. A series of Pebax® block copolymers, containing varying proportions of soft poly(tetramethylene oxide) and hard poly(amide-12), was evaluated to determine the effect of hard segment proportion on solute affinity toward two biotransformation target molecules, carveol and carveone. Subsequently, representative homopolymers comprising the copolymers' soft segment were examined individually for the effects of molecular weight, crystallinity, and polymer end group polarity on affinity.

RESULTS: Partition coefficients decreased with greater proportions of copolymer hard segments and homopolymer crystallinity, both of which act as non-absorptive domains, but which impart mechanical strength to the polymer. Partition coefficients increased with decreasing homopolymer molecular weight, which was ascribed to increased entropy of mixing. Hydroxyl vs. ether end group functionality had a variable effect on the partitioning of polar and non-polar solutes, providing a basis for the rational design of selective oligomeric absorbents.

CONCLUSION: Block copolymers can provide an attractive, low-cost option for polymeric sequestering phases in TPPBs, but commercial grades of these materials are not optimized for these applications. TPPB performance can be improved by selecting/fabricating polymers that minimize the molecular weight of the soft component, the proportion of hard segment, and by considering the effects of end group composition.

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Keywords: bioseparations; extraction; fermentation; reactor design; sorption; thermodynamics

INTRODUCTION

Block copolymers comprised of discreet hard and soft 'blocks' of substantially different composition are effective absorbents for *in situ* product removal (ISPR) in two-phase partitioning bioreactors (TPPBs), and can also be applied for substrate delivery in biodegradative applications. Block copolymers provide the soft, amorphous phase needed for solute absorption and the glassy and/or semi-crystalline 'hard' phase that provides the mechanical integrity needed to withstand autoclaving and agitation in bioreactor vessels.^{1–3} The materials of interest for TPPB applications have generally been thermoplastic elastomers, with the soft segment comprising the continuous phase; without the presence of the 'hard' phase these material would exist as amorphous liquids above their glass transition temperature (T_g) under TPPB conditions.

Commercially-available block copolymers are much less expensive than alternative sequestering phases such as specialized resins or liquid solvents,⁴ and the mechanism of solute absorption by these polymers has been shown to be identical to solvent extraction, namely, absorption. While these materials are

developed to provide thermo-mechanical properties that satisfy engineering requirements (e.g. automobile parts), little is known about the structure–property relationships that govern their interactions with small molecules and that would therefore dictate their performance in TPPB applications.

The Pebax® series of poly(ether-block-amide) materials produced by Arkema are among the most thoroughly-characterized block copolymers. Reports of their mechanical and thermal properties^{5–9} have been augmented with studies of their transport properties in membrane separations^{10–15} and in drug delivery systems.^{16–18} The Pebax® grades of present interest have soft blocks comprised of poly(tetramethylene oxide) (PTMO) that provide a glass transition (T_g) near -70°C and melting

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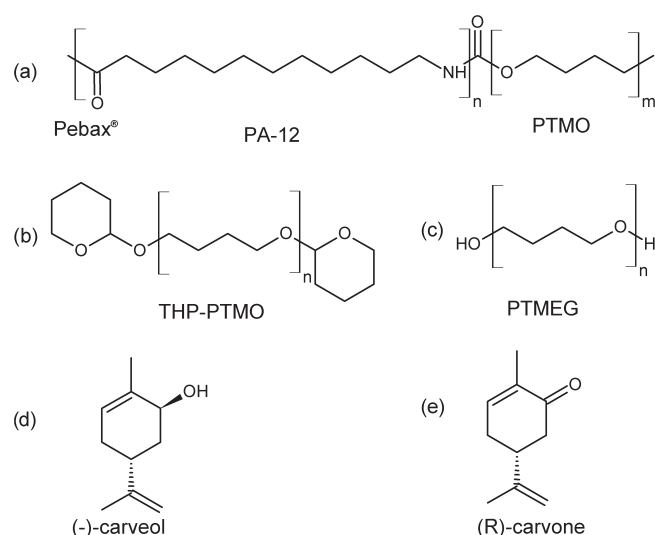


Figure 1. Chemical structures of the absorbent polymers: (a) Pebax[®]; (b) THP-PTMO; (c) PTMEG; and target molecules of interest: (d) carveol; (e) carvone.

Table 1. Properties of Pebax[®] '33' block copolymer series. Poly(amide-12) (PA-12) is the hard segment component, and poly(tetramethylene oxide) (PTMO) is the soft segment component

Pebax [®] grade	2533	3533	4033	7033
PA-12 wt% ^{7,10}	12	13	27	73
PTMO wt% ^{7,10}	84	83	70	25
T _g (°C) (PA-12)*	70	68	65	62
T _m (°C) (PA-12)*	142	149	165	175
T _g (°C) (PTMO)*	-76	-72	-65	ND
T _m (°C) (PTMO)*	12	11	7	ND
Water absorption (%)	1.2 ²⁸	1.2 ²⁹	1.2 ³⁰	1.1 ³¹
Hardness (Shore D)	27 ²⁸	33 ²⁹	42 ³⁰	70 ³¹
Strain at break (%)	>750 ²⁸	>600 ²⁹	>450 ³⁰	>350 ³¹

ND: Not determined
*This study

temperatures (T_m) less than 25°C (Fig. 1). The hard blocks are comprised of poly(amide-12) (PA-12), that provide T_g's near 70°C and melting temperatures in excess of 130°C.^{5,10,11} The immiscibility of these blocks produces a phase-separated morphology, wherein one block component forms the continuous phase, and the other resides in dispersed domains.⁷ Table 1 is a summary of the composition and thermo-mechanical properties of the Pebax[®] materials examined in this work. Note that of the four copolymers, only Pebax[®] 7033 appears to have a continuous polyamide phase, as indicated by its relatively high shore D hardness.

These Pebax[®] materials were selected based upon their different proportions of hard and soft blocks, to determine the influence of copolymer composition on the affinity towards carveol and carvone, the inhibitory substrate and natural aroma product of a biotransformation previously examined in a TPPB context, whose structures are given in Fig. 1(d) and 1(e), respectively. These target molecules must be separated from the aqueous phase to avoid biocatalyst inhibition, yet some selectivity toward carvone is favourable to provide a sufficient aqueous carveol concentration to drive enzymatic conversion.¹⁹

Our study begins with partition coefficient (PC) measurements to establish the sorption capacity of each Pebax[®] copolymer domain. Subsequently, a series of tetrahydropyranl ether-terminated poly(tetramethylene oxide) (THP-PTMO, Fig. 1) materials of varying molar mass are prepared and investigated to isolate the effect of molecular weight on partition coefficients. Finally, a series of hydroxyl-terminated poly(tetramethylene ether glycol) (PTMEG, Fig. 1) polymers are examined to explore the influence of end-group composition on the sorption of carveol and carvone.

The results of this study are useful to shape future TPPB polymer selection / design strategies, which should shift towards application-specific materials. By incorporating the findings of this study in terms of controlling properties such as molecular weight, end group composition, and crystallinity, the performance of TPPB sequestering phases should be better predicted and improved.

MATERIALS AND METHODS

Chemicals

(-)-Carveol (mixture of isomers), (R)-(-)-carvone, p-toluenesulfonic acid monohydrate, and 3,4-dihydro-2H-pyran (DHP) were purchased from Sigma-Aldrich (Canada). Hydroxyl-terminated poly(tetramethylene ether glycol) (PTMEG) samples with average molecular weights of 250, 650, 1000, 2000, and 2900 g mol⁻¹, designated PTMEG followed by their molecular weight, were purchased from Scientific Polymer Products (Ontario, NY, USA). Pebax[®] grades 2533, 3533, 4033, and 7033, all medical grade and additive-free, were used as received from Foster Corporation (Putnam, CT, USA), while poly(amide-12) was used as donated by DuPont Canada.

THP-terminated poly(tetramethylene oxide) (THP-PTMO)

Etherification of the hydroxyl end groups within PTMEG samples was accomplished by acid-catalyzed reaction with DHP in dilute solution. In a round-bottom flask, the amount of PTMEG of a certain molecular weight was chosen to provide an equivalent end group concentration across the molecular weight range. The polymer was dissolved in dichloromethane (18 mL), before adding DHP (2 g) and p-toluenesulfonic acid (9 mg). The resulting cement was stirred for 16 h at room temperature, washed with a saturated NaHCO₃ solution (20 mL), and dried over anhydrous Na₂SO₄. Residual solvent was removed by rotary evaporation, followed by short-path Kugelrohr distillation under high vacuum (25°C) to give THP-PTMO samples as clear, pale yellow oils of varying viscosity. ¹H NMR analysis (CDCl₃): δ 4.52 (dd, -O-CH(O)-CH₂, 1H), δ 3.79 and 3.67 (dt, -O-CH₂(6-THP), 2H), δ 3.34 (m, THP-O-CH₂-CH₂-, 2H), δ 3.28 (m, -CH₂-O-CH₂-, 4(n-1)H), δ 1.80-1.43 (m, -CH₂-CH₂-CH₂(3,4,5-THP) and aliphatic -CH₂-CH₂-, (12+4n)H), N being the average number of monomer units present in the polymer, which was calculated as being between 3 and 4 for the sample derived from 250 g mol⁻¹ PTMEG, whose ¹H NMR spectrum is shown in Supplement Figure S1.

Thermodynamic modeling of partition coefficient

The partition coefficient is defined as the ratio of the equilibrium concentrations of the solute in the polymer (w_i^{nap}) and aqueous (w_i^{aq}) phases, and is described in thermodynamic terms by the ratio of solute activity coefficients:

$$\text{Partition Coefficient} = \frac{w_i^{\text{nap}}}{w_i^{\text{aq}}} = \frac{\Omega_i^{\text{aq}}}{\Omega_i^{\text{nap}}} \quad (1)$$

In this equation, Ω_i^{aq} and Ω_i^{nap} are weight-fraction activity coefficients, which were calculated from mole-fraction coefficients (γ_i) using the equation:

$$\Omega_i = \gamma_i \frac{x_i}{w_i} \quad (2)$$

where γ_i is the mole-fraction activity coefficient and x_i is the solute mole fraction in the phase of interest. The aqueous-phase activity coefficients of carvone and carveol ($\gamma_{\text{carvone}}^{\text{aq}} = 6310$, $\gamma_{\text{carveol}}^{\text{aq}} = 2920$) were literature values reported at infinite dilution.²⁰ Polymer-phase values were calculated using the Flory Huggins relation:

$$\ln \gamma_i^{\text{pred}} = \ln \frac{\varphi_i}{x_i} + 1 - \frac{\varphi_i}{x_i} + \chi_{ij} \varphi_j^2 \quad (3)$$

This equation requires knowledge of polymer and solute molar volumes (Φ_i), as well as the binary interaction parameter (χ_{12}) discussed above. Unfortunately, Flory Huggins interaction parameters for poly(tetramethylene oxide) and the solutes of interest are unavailable, forcing us to use semi-empirical correlations to estimate the binary mixture parameter from pure-component data. We selected the approach using Hansen Solubility Parameters²¹ described by Lindvig *et al.*,²² which provides χ_{12} from dispersive (δ_{di}), polar (δ_{pi}), and hydrogen bonding (δ_{hi}) parameters, as follows.

$$\chi_{12} = \alpha \frac{V_1}{RT} \left[(\delta_{d1} - \delta_{d2})^2 + 0.25 (\delta_{p1} - \delta_{p2})^2 + 0.25 (\delta_{h1} - \delta_{h2})^2 \right] \quad (4)$$

The Hansen parameters for poly(tetramethylene oxide) are ($\delta_d=16.2$, $\delta_p=3.3$, $\delta_h=2.2$), while those of carveol are ($\delta_d=17.3$, $\delta_p=4$, $\delta_h=9.2$) and carvone are ($\delta_d=17.2$, $\delta_p=6.9$, $\delta_h=4.2$). Using $\alpha=1.0$, Equation (4) gives $\chi_{12} = 0.499$ for poly(tetramethylene oxide)/carveol and $\chi_{12} = 0.154$ for poly(tetramethylene oxide)/carvone. A lower χ_{12} value indicates more favourable solute/polymer interactions. The difference between the predicted solute/polymer interaction parameter values encapsulates the relative enthalpic interactions, with carvone exhibiting more favourable interaction with PTMO than carveol.

Partition coefficient experiments

Partition coefficients (PC) were determined by contacting a known mass of polymer with stock solute solutions under agitation at 180 rpm. The contact time was 48 h unless stated otherwise. While ideal experimental conditions would yield infinitely dilute solute concentrations in both phases,²³ analytical measurement limitations required solute concentrations to be varied based on polymer absorption capacity. For this reason, c. 0.3 g of polymer was contacted with carveol/carvone solutions of approximately 500 mg L⁻¹ each. Aqueous samples were withdrawn and passed through a 0.2 μm nylon syringe filter prior to HPLC analysis of the aqueous phase solute concentration. The concentration in the polymer phase was calculated by mass balance, assuming negligible losses. All partition coefficient experiments were conducted in triplicate, and reported values are the average with error bars representing one standard deviation from the mean. Reported values are specified in the figures as being measured directly, or normalized to the PTMO fraction in Pebax[®] or the non-crystalline fraction in PTMEG using:

$$PC_{\text{norm}} = \frac{PC_{\text{obs}}}{1 - X_c} \quad (5)$$

where PC_{norm} denotes the normalized partition coefficient, PC_{obs} denotes the experimental value, and X_c denotes the fraction of the material which is composed of crystalline and/or glassy domains.

Analytical methods

¹H NMR spectra were acquired in CDCl₃ with a Bruker AM-400 instrument, with chemical shifts referenced to the residual proton resonance of chloroform. DSC analysis was conducted using a TA Instruments Q100 at a heating rate of 10°C min⁻¹, with results reported for the first heating to assess samples as used in partition coefficient determinations. Degree of crystallinity was determined by dividing the integrated melting endotherm by the specific heat capacity of an ideal crystal; 172.2 J g⁻¹ for PTMEG²⁴; and 245 J g⁻¹ for poly(amide-12).²⁵

Aqueous solute concentrations were measured by HPLC using a Varian Polaris C18-A 150×4.6 mm 5 μm column and a Varian ProStar 325 UV detector operating at 200 nm. The mobile phase for carveol/carvone analysis was 50:50 acetonitrile:water at 1 mL min⁻¹, with both carveol isomers eluting at 5.5 min, and carvone at 7 min.

RESULTS AND DISCUSSION

Pebax[®] series: influence of hard/soft segment proportions

As discussed above, block copolymers exist in a phase-separated morphology comprised of a continuous and a dispersed phase, arising from inability of the component blocks to mix and form a solution. The distribution of each phase, being either dispersed (isolated domains) or continuous (uninterrupted), is dependent on the abundance of each block component, among other factors. In the context of solute absorption, this blend morphology complicates attempts to predict and/or measure the affinity of each homopolymer component for the target molecule.^{5,9} In an effort to understand the effect of copolymer composition on solute uptake, a series of Pebax[®] grades were examined (Table 1), which ranged from a 12/86 distribution of hard/soft blocks in the softest grade, P2533, to 73/25 in the hardest grade, P7033.

The data reported in Table 2 demonstrate the remarkable affinity of Pebax materials for both carvone and carveol, as partition coefficients for the softest copolymer grades generally exceeded 155. Moreover, solute uptake correlated strongly with copolymer composition, as increases in polyamide content from 12 wt% to 73 wt% reduced the partition coefficients by a factor of seven. The lower absorptive capacity of the polyamide block relative to

Table 2. Partition coefficients (measured directly, and normalized to the soft PTMO fraction given in Table 1) for carveol and carvone

Polymer	Carveol PC	Carvone PC	Carveol PC normalized ^c	Carvone PC normalized ^c
Pebax [®] 2533 ^a	154.7 ± 3.9	157.0 ± 2.2	184	187
Pebax [®] 3533 ^a	152.1 ± 1.9	151.1 ± 0.5	182	180
Pebax [®] 4033 ^a	123.0 ± 1.2	108.9 ± 1.5	175	155
Pebax [®] 7033 ^a	22.2 ± 2.9	21.9 ± 2.9	89	88
PA-12 ^a	0.8 ± 0.4	0.4 ± 0.4	---	---
PA-12 ^b	4.5 ± 0.8	4.6 ± 0.8	---	---
THP-PTMO-990 ^a	163.9 ± 1.5	214.4 ± 6.7	---	---
THP-PTMO-990 ^b	147.3 ± 8.2	192.5 ± 9.6	---	---

^a PC measurements acquired after 48 h contact between polymer and aqueous solute solution.

^b PC measurements acquired after 14 days contact between polymer and aqueous solute solution.

^c Normalized by dividing PC by the PTMO fraction in the block copolymer.

the polyether block was confirmed by analysis of the respective homopolymers. Whereas ether-terminated poly(tetramethylene oxide) with a molecular weight of 990 g mole⁻¹ (THP-PTMO-990) provided PC values of 214 for carvone and 163 for carveol, a sample of polyamide-12 (PA-12) provided values of just 0.8 and 0.4 for these respective solutes.

These results are consistent with previous reports of the importance of glass transition temperature on solute uptake. THP-PTMO-990 is an amorphous material with a T_g below room temperature, whereas PA-12 is semi-crystalline with a T_g of approximately 40°C. Given that crystalline domains are non-absorptive, and glassy domains lack the molecular mobility needed for rapid solute uptake, the relatively poor performance of the PA-12 blocks after 48 h of solute solution contact is not surprising. Note that increasing the extraction time to 2 weeks improved the PC values for PA-12 to 4.5 for carveol and 4.6 for carvone, while the PC values measured after 2 weeks of contact with THP-PTMO-990 were similar to those seen after 48 h. The slow evolution of sorption capacity by PA-12 is likely the result of polymer plasticization by solute and/or water, which lowers T_g to the point where solute uptake is more kinetically favorable.²⁶

Further insight was gained by normalizing the PC data for each Pebax material by dividing by the fraction of PTMO in the block copolymer. If the polyether phase dominates target molecule absorption, then these normalized values should be constant. The results listed in Table 2 show this behaviour for the soft Pebax[®] grades 2533, 3533, and 4033. Moreover, the normalized values were consistent with those measured for the ether homopolymer, THP-PTMO-990. However, the normalized partition coefficient values for Pebax[®] 7033 were significantly lower, indicating that the polyether soft block in this material was much less absorptive than expected based on its composition. This is probably due to phase morphology, as for this polymer the high PA-12 content now produces a continuous phase comprised of polyamide, and a dispersed phase of polyether. This morphology presents a kinetic barrier to absorption by the soft segment, thereby reducing both experimental and normalized PC values.

Note that the hard segment impedes solute uptake, but also does provide the mechanical integrity required for polymeric TPPB applications. THP-PTMO-990 is a viscous oil at standard bioreactor temperatures, whereas Pebax[®] 2533 is a solid due to the blend morphology provided by the PA-12 phase. The mechanical resilience of these Pebax[®] grades is maintained up to the melting point of PA-12 domains, which in the present case exceeds the temperatures commonly used in autoclave sterilizations. Given the need to balance thermo-mechanical properties with solute uptake capacity, an effective block copolymer composition is one whose soft segment is optimized on the basis of solute affinity, and whose hard segment is selected on the basis of its effect on mechanical properties. Ideally, the hard segment can also be absorptive, such as in semi-crystalline polymers with melting points in excess of sterilization temperatures and glass transitions lower than bioreactor operating room temperatures.

Rational design of soft segment composition and molecular weight

The remarkable performance of ether-rich grades of Pebax[®] for the sorption of carveol and carvone is the product of several factors stemming from the poly(tetramethylene oxide) phase. Most importantly, the soft segment is amorphous and above its T_g at bioreactor operating temperatures, thereby avoiding complications associated with a non-absorptive crystalline phase

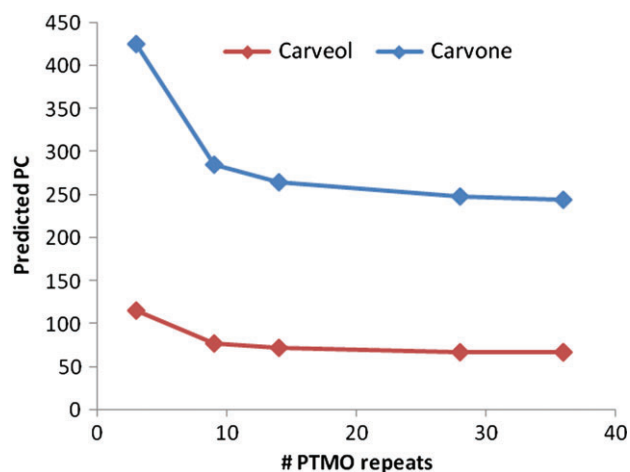


Figure 2. Predicted partition coefficients of carvone and carveol in PTMO using the Flory Huggins-Hansen thermodynamic activity model.

as well as the poor transport properties provided by a glassy phase below its T_g . As such, soft segment design must begin with a consideration of phase transition temperatures observed in the field of TPPB use. Semi-crystalline and glassy polymers may be effective when water and/or solute reduces the glass transition temperature by plasticization, or suppresses the melting point below 30°C, yielding an absorptive, rubbery material.

Beyond these phase transition considerations, soft segment selection is concerned with affinity for the target molecule, as dictated by equilibrium thermodynamic principles. Bacon *et al.* have reviewed the various means of predicting the equilibrium distribution of a solute between aqueous and polymeric phases using relatively simple activity coefficient models and their various proxies.²⁶ The simplest approach utilizes the Flory Huggins theory to calculate the activity coefficient of the solute in the polymer phase, assuming that the material does not absorb water and can, therefore, be modeled as a binary system. The challenge in applying this approach is to find values of the Flory Huggins parameter (χ_{12}) for the solute–polymer combination of interest. While such data are often lacking, χ_{12} can be estimated from more plentiful Hildebrand and Hansen solubility parameter data. With such estimates, the influence of polymer composition and molecular weight on solute partitioning can be predicted.

Figure 2 is a plot of the predicted partition coefficients for carveol and carvone absorption into poly(tetramethylene oxide) at 30°C as a function of polymer molecular weight. The data are remarkable in two respects. First, the predicted PC values are of the same order of magnitude as experimental values, confirming that simple thermodynamic models are reliable screening tools for selecting/designing TPPB absorbents. Sources of the discrepancy between predicted and measured values include the oversimplification of non-ideal polymer/solute interactions that are inherent in using pure component Hansen parameters to estimate χ_{12} , as well as the potential for poly(tetramethylene oxide) to absorb water from the aqueous phase, rendering the polymer phase a ternary mixture (polymer + solute + water) as opposed to a binary (polymer + solute) system.

Second, the model predictions suggest that partition coefficients improve significantly upon moving to lower molecular weights. This trend arises from the entropic effects associated with the mixing of the solute with increasingly smaller polymer chains. To clarify, entropic contributions to mixing arise from the number

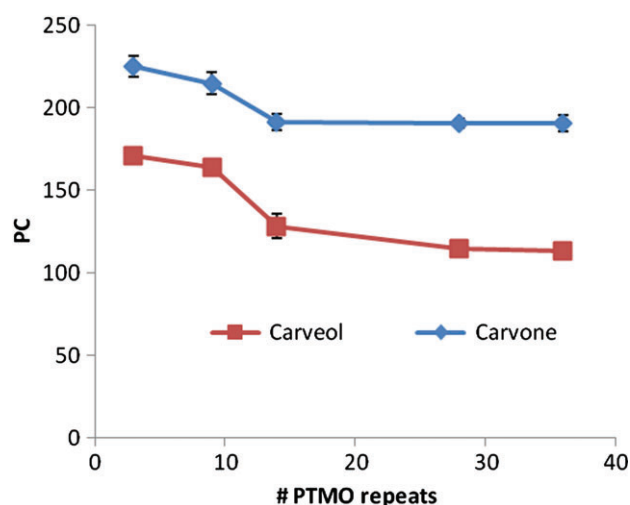


Figure 3. Partition coefficients of carveone and carveol in the THP-PTMO series with increasing molecular weight.

of possible conformations of the polymer and solute as they occupy a given space, which increase with a reduction in molecular weight. This trend is observed experimentally, as shown in Fig. 3 for solute absorption by THP-PTMO materials of different degrees of polymerization. Experimental partition coefficients were nearly constant above approximately 1000 g mol^{-1} , but increased by up to 50% at lower molecular weights.

The improvement in PC values arising from reducing polymer chain length suggests that future efforts in the design or selection of TPPB extractants should consider oligomeric materials. However, the physical state of a polymer affects its potential utility as an extractant. Solid polymers, characterized by high molecular weight, have been valued as TPPB extractants for their inertness with respect to many biocatalysts, while perhaps the main problem with using immiscible liquid solvents as extractants is their non-biocompatibility due to interactions with the biocatalyst in the aqueous phase. Therefore, if lower MW polymers are to be selected for their anticipated higher partitioning, it will also be necessary to determine any effects on biocompatibility, which is a study currently underway in our laboratory.

In the design of custom block copolymers, the incorporation of low molecular weight polymers chosen specifically for their affinity as soft blocks in block copolymers, while including a sufficient proportion of hard blocks to provide physical integrity, may improve the affinity of the soft segment relative to the commercial materials, which are currently designed primarily for their physical properties. The molecular weight effect in the Pebax[®] system is expected to be small, due to the covalent tethering of the soft segment to the PA-12 hard segment, increasing chain rigidity and effective molecular weight.

Effect of end-group composition on solute affinity

The composition of polymer end-groups is rarely considered in the context of solute absorption, especially when high molecular weight polymers are employed. However, as molecular weights are reduced and/or microstructures involving a high degree of branching are generated, the increased concentration of end-groups provides an opportunity to affect solute uptake substantially. In the present case, the THP-PTMO series of polymers contained non-polar ether functionality akin to that present in the polymer backbone. These materials were clear, liquid oils that lacked any

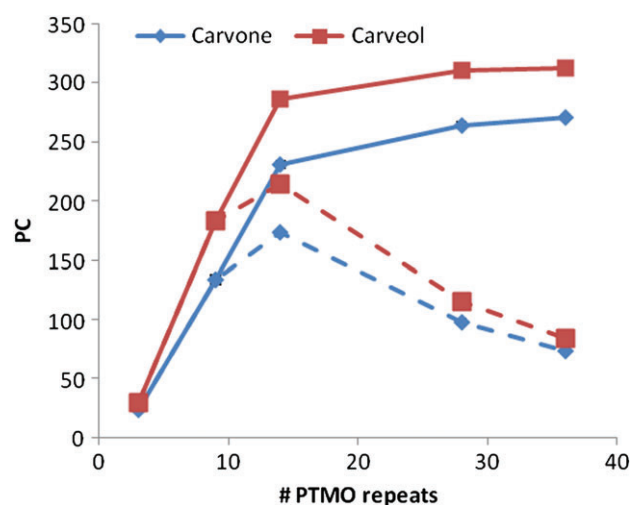


Figure 4. Partition coefficients of carveone and carveol in the PTMEG series with increasing molecular weight. Solid lines represent values normalized to amorphous portion measured by DSC. Dashed lines represent values measured directly.

discernable degree of crystallinity, much like the soft segments present within Pebax[®].

The chemical precursors of the THP-PTMO series were telechelic hydroxyl-terminated materials (HO-PTMO, PTMEG) that were cloudy liquids in the 250–650 molecular weight range, and waxy solids of increasing hardness as molecular masses exceeded 1000. The effect of end-group composition on the degree of crystallinity was unexpected, as end-groups do not pack within crystallites that are comprised of polyether chain segments. The difference in crystallinity between THP-PTMO and HO-PTMO may arise from differences in the entropy of melting, with the association of polar hydroxyl functional groups serving to reduce the degree of randomness gained upon passing from the crystalline to the melt state. Irrespective of its cause, the degree of crystallinity varied considerably with molecular weight, as indicated in Fig. 4 by the dramatic reduction in PCs measured at higher degrees of polymerization. Because crystallites are unable to absorb solutes, a better measure of the thermodynamic affinity of a polymer composition toward a solute is one that reflects the absorptive capacity of its amorphous phase alone. This is accomplished by normalizing experimental partition coefficients by dividing by the amorphous (non-crystalline) fraction of the material.²⁷

Two clear effects arising from the effect of end-group composition are apparent in comparing the PC results for THP-PTMO in Fig. 3, with those for PTMEG shown in Fig. 4. First, the polarity contributed by the hydroxyl end groups of PTMEG causes a dramatic decrease in polymer affinity towards the target molecules carveol and carveone at molecular weights below 1000 g mol^{-1} . The hydroxyl end-group functionality present in the PTMEG series imparts significant polarity, and the magnitude of the contributed polarity depends on the amount of chain end groups relative to repeat units within the chain at various molecular weights; that is, the hydroxyl ends will contribute relatively more overall polarity to a very short PTMEG chain than to a longer one which is comprised mainly of relatively non-polar tetramethylene oxide functionality. This phenomenon is contrary to and much stronger than the effect of molecular weight on partition coefficients shown in the THP-PTMO polymer series (Fig. 3), which was attributed to entropic effects in the absence of enthalpic end group effects. In the case

of the hydroxyl-terminated PTMEG polymer series, while the same entropic effect at low molecular weights is presumably at play, it is clearly overshadowed by the effect of end group composition which acts to decrease the polymer's affinity towards the relatively hydrophobic target molecules, carveol and carvone, at low molecular weights.

The second effect of end group polarity is its influence on target molecule selectivity, seen by the inversion of relative affinity towards carveol and carvone between the THP-PTMO and PTMEG series in Figs 3 and 4, respectively. This significant difference in relative PC values, which is constant across the tested molecular weight range, illustrates the phenomenon of 'like dissolves like'. Carveol's greater polar surface area relative to carvone (20.23 Å² vs. 17.07 Å²), owing to its hydroxyl functionality, potentially imparts favourable affinity towards the more polar PTMEG due to its hydroxyl end group functionality, while carvone exhibits greater affinity towards the non-polar THP-PTMO.

This feature provides a strategy to improve affinity by selecting chain end functionality in commercial or custom-designed polymers, especially with low molecular weight polymers, and may also be useful in achieving selectivity among several target molecules. Interestingly, the Pebax[®] series of copolymers do not exhibit such selectivity, with PC values for both carveol and carvone being approximately equal (Table 2). In the copolymer material, segments are tethered at either end to join the discreet blocks, and free ends may be terminated or degraded. The results indicate that the manipulation of chain end group composition provides an additional, useful variable in TPPB extractant selection to adjust target molecule affinity and selectivity; however, the effect of chain-end composition has additional implications for polymer physical properties, as shown above with the degree of crystallinity.

CONCLUSIONS

Block copolymers containing a large proportion of soft, amorphous segments are effective absorbents for TPPB applications due to their favourable affinity conferred by the soft segments in combination with good mechanical and thermal properties conferred by the hard segments, which do not significantly absorb solute, and whose proportion in sequestering materials should be as small as practically possible.

The non-polar end group functionality in the THP-PTMO series demonstrates that a reduction in molecular weight improves solute affinity by increasing the entropy of mixing, which is consistent with thermodynamic predictions. The presence of hydroxyl end groups in the PTMEG series demonstrates that polar end groups impart relatively more polarity at lower molecular weights, hindering affinity toward non-polar target molecules, and possibly increasing mutual polymer–water solubility.

This study has identified useful strategies for future extractant selection efforts, which are intended to improve on currently-available materials through modifications or the design of task-specific materials. Reductions in molecular weight, crystallinity, and hard segment proportion all act to improve solute partitioning at the expense of physical properties, while polymer polarity offers a tool for target molecule selectivity. Future investigations by our Group aim to characterize the potential consequences of the above-mentioned aspects on biocompatibility, and to elucidate the effects on mass transfer rates, two important considerations in bioprocess design.

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Supporting Information

Supporting information may be found in the online version of this article.

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