Supplemental Information for

Latanoprost Uptake and Release from Commercial Contact Lenses

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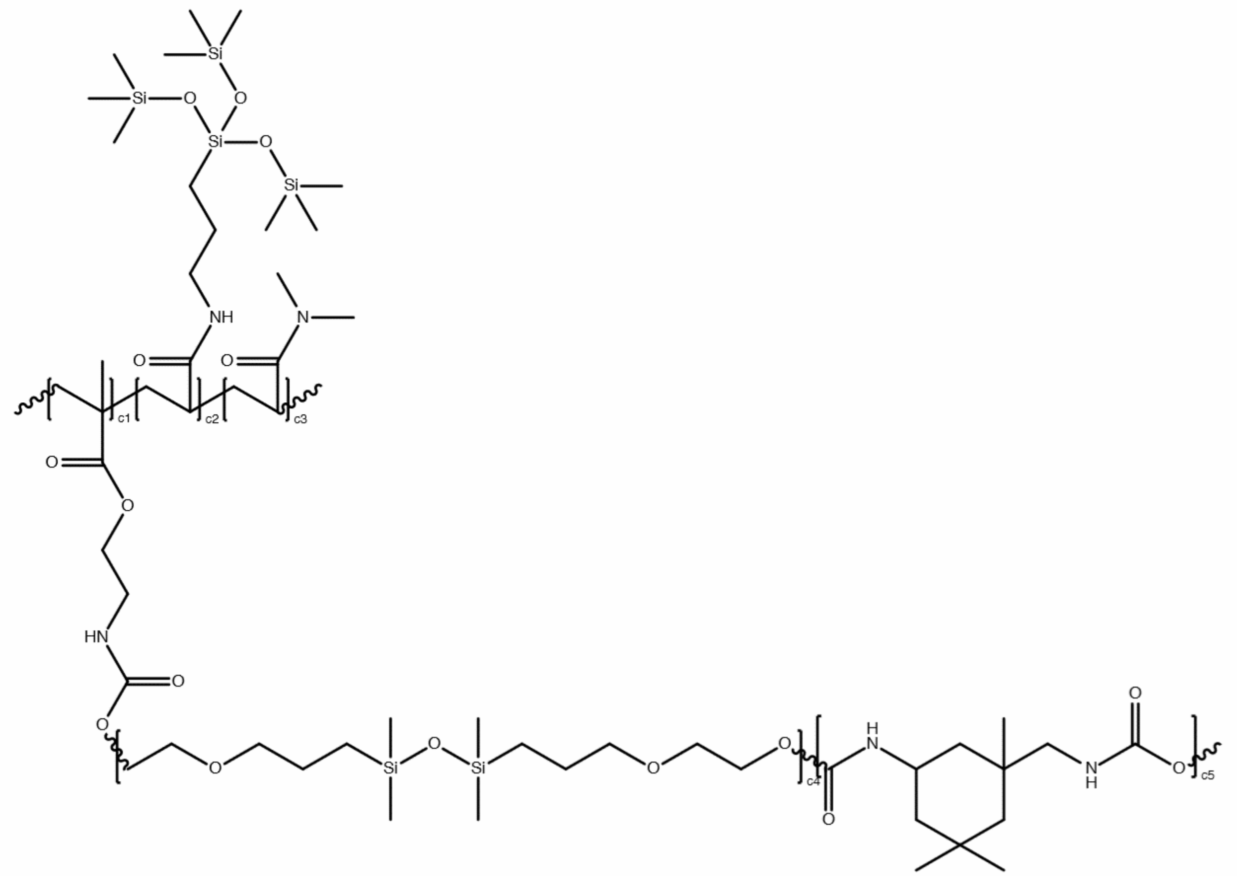
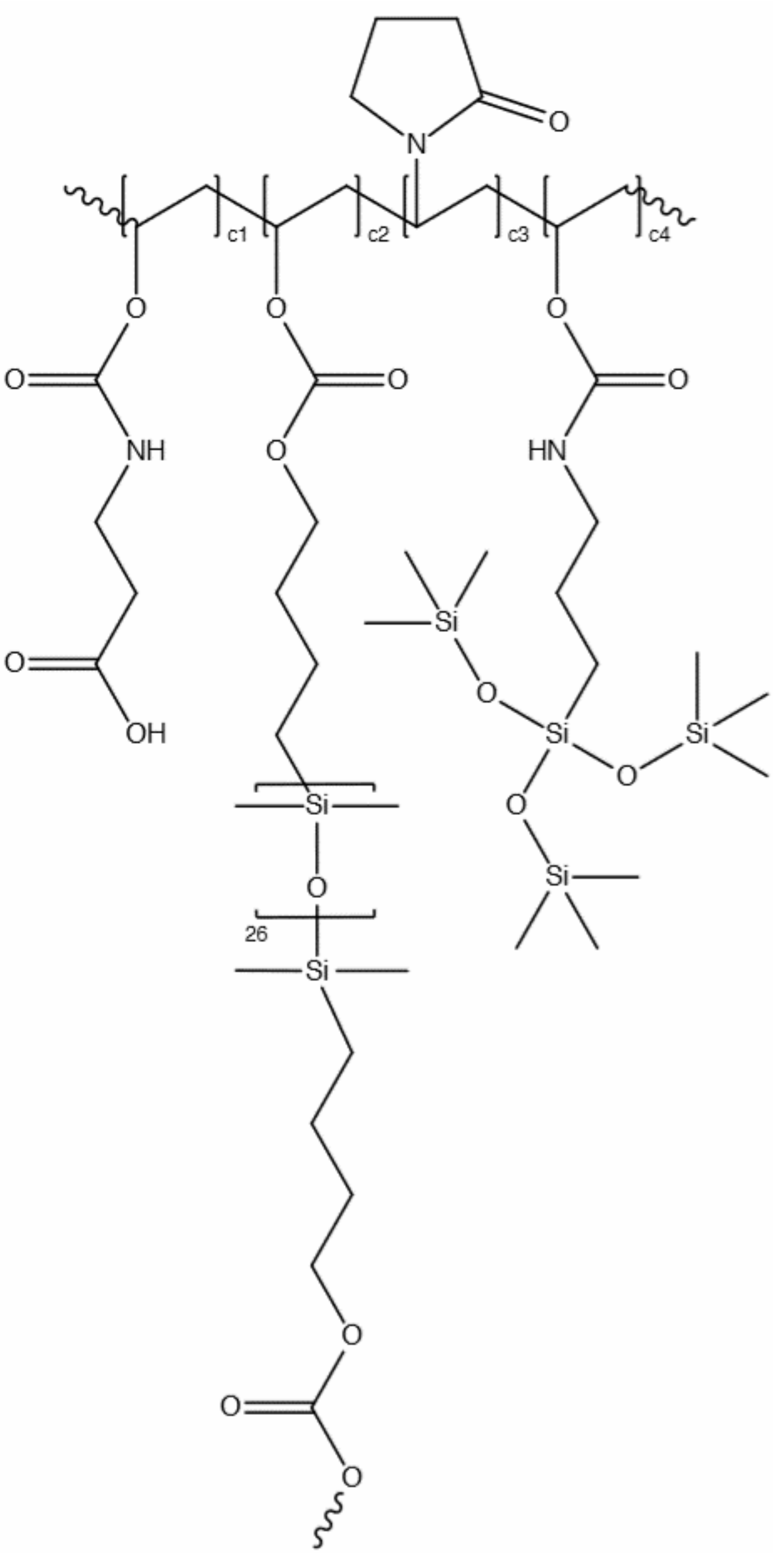
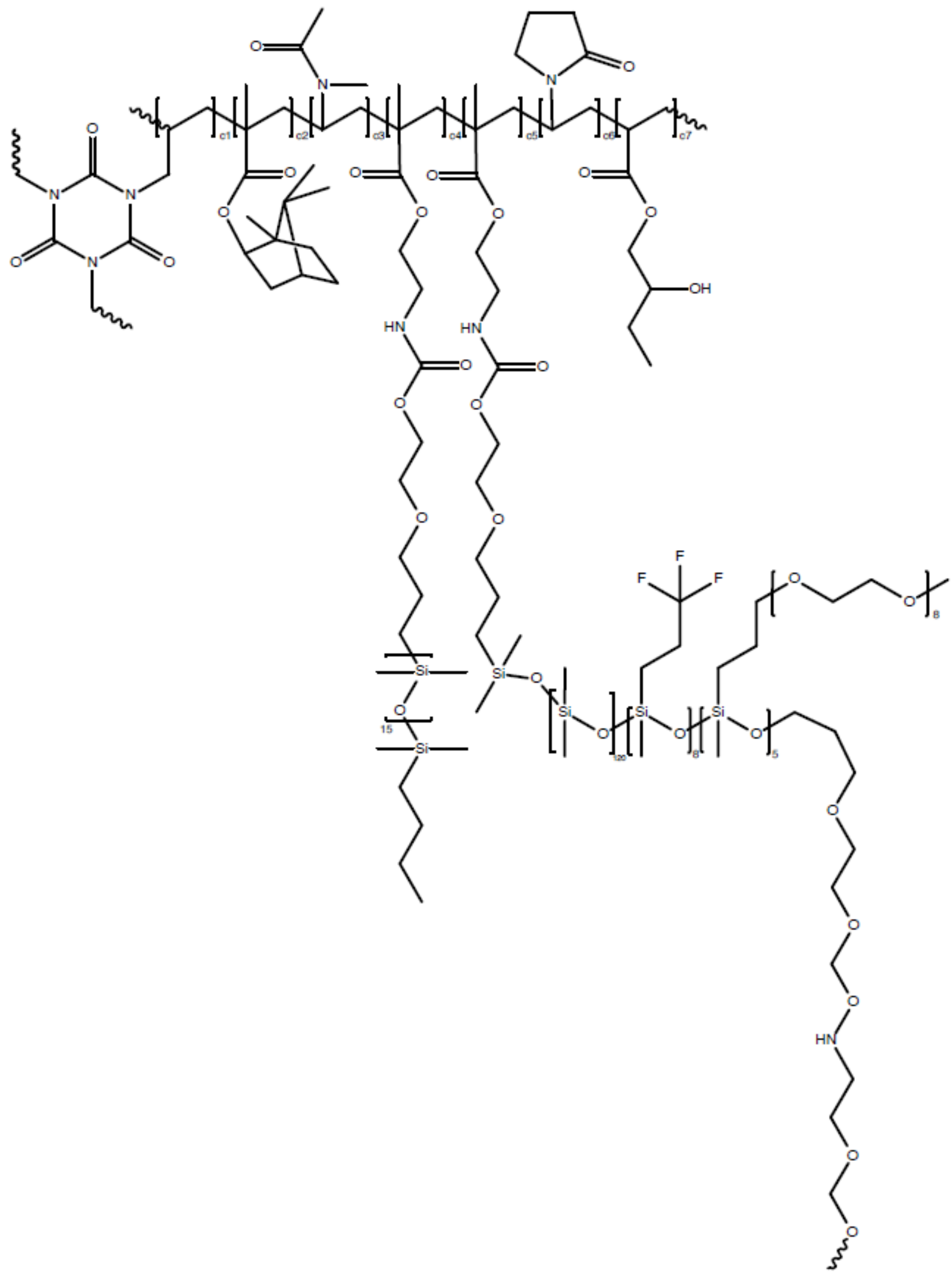
1 Proposed structure of commercial contact lens materials



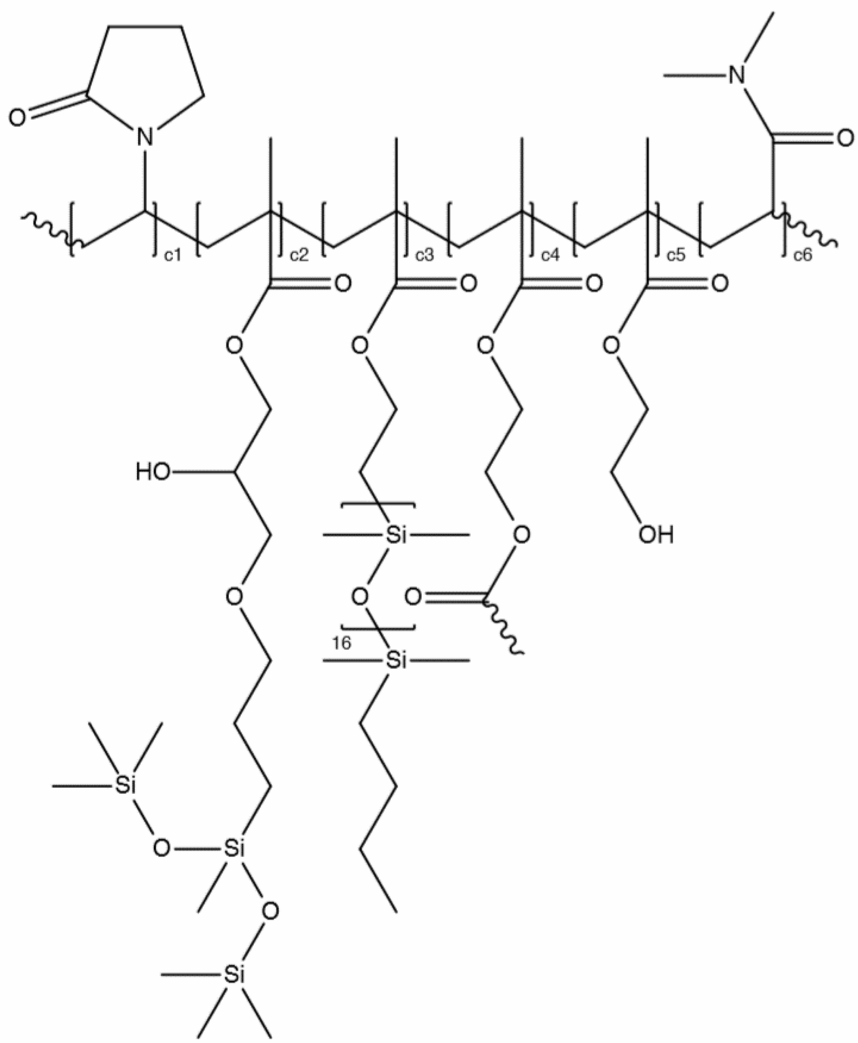
Supplemental Figure S1. Proposed average repeat unit molecular structure of **Delefilcon A**. The estimated mole fractions of the repeat structures of CM3, CM2, CM5, CM1, and CM4 are respectively 0.1662, 0.0702, 0.5772, 0.0749, and 0.1116, corresponding to symbols c1, c2, c3, c4, and c5. [1] Oscillating lines represent crosslinking connections to the network.



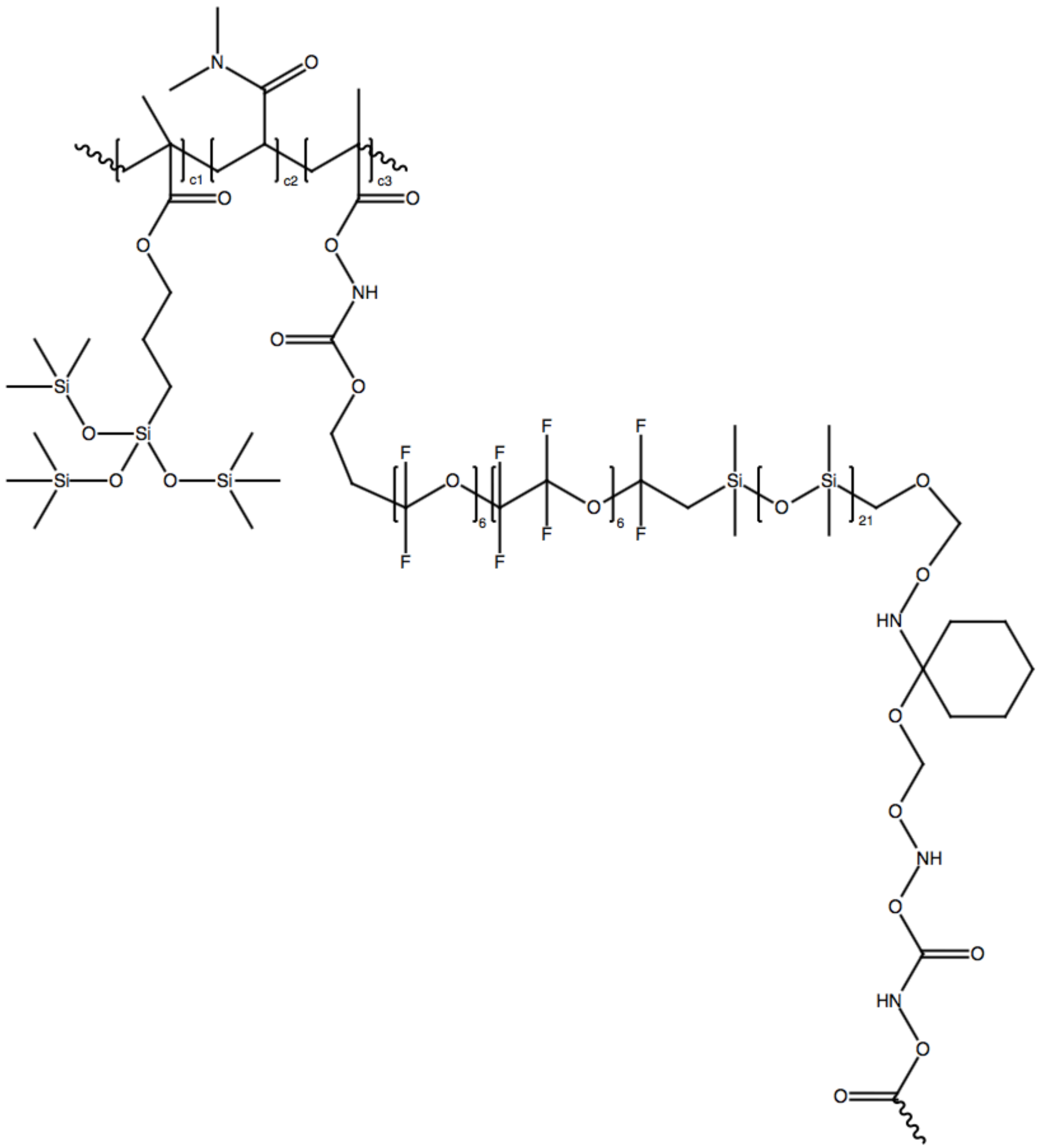
Supplemental Figure S2. Proposed average repeat unit molecular structure of **Balafilcon**. The estimated mole fractions of the repeat structures of NVA, PBVC, NVP, and TPVC are respectively 0.5224, 0.0765, 0.299, and 0.102, corresponding to symbols c1, c2, c3, and c4. [2,3] Oscillating lines represent crosslinking connections to the network.



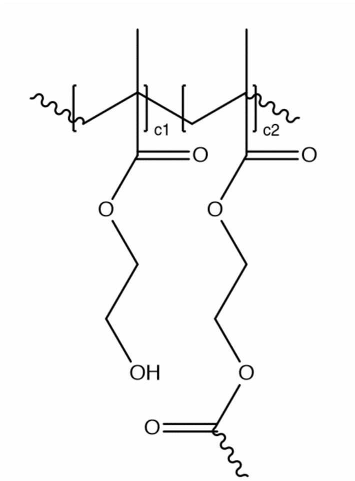
Supplemental Figure S3. Proposed average repeat unit molecular structure of **Comfilcon A**. The estimated mole fractions of the repeat structures of TAIC, IBM, VMA, FM0411M, M3U, NVP, and HOB are respectively 0.0149, 0.1438, 0.3224, 0.0194, 0.0099, 0.2876, and 0.2021, corresponding to symbols c1, c2, c3, c4, c5, c6, and c7. [3] Oscillating lines represent crosslinking connections to the network.



Supplemental Figure S4. Proposed average repeat unit molecular structure of **Galyfilcon A**. The estimated mole fractions of the repeat structures of PVP, SiGMA, mPDMS, EGDMA, HEMA, and DMA are respectively 0.1747, 0.1102, 0.0407, 0.0123, 0.0746, and 0.5875, corresponding to symbols c1, c2, c3, c4, c5, and c6. [3,4] Oscillating lines represent crosslinking connections to the network.



Supplemental Figure S5. Reported average repeat unit molecular structure of **Lotrafilcon B**. The corresponding mole fractions of the repeat structures of TRIS, DMA, and Siloxane Macromer are respectively 0.8503, 0.0997, and 0.0500, corresponding to symbols c1, c2, and c3. [3,5,6] Oscillating lines represent crosslinking connections to the network.



Supplemental Figure S6. Proposed average repeat unit molecular structure of **Polymacon**. The estimated mole fractions of the repeat structures of HEMA and EGDMA are respectively 0.9917 and 0.0083, corresponding to symbols c1 and c2. [3] Oscillating lines represent crosslinking connections to the network.

2 Calculation of solubility parameters

For certain contribution groups not conventionally found in the HVK group contributions, we used parameters from Meaurio et al., who created group contributions for some additional groups.[7] For poly(dimethyl siloxane) (PDMS) we created group contribution parameters based on experimental Hansen solubility parameters found in Smith.[8] For the single silicon atom (>Si<), we assumed it had the same group contribution as a carbon atom (>C<), but with the molar volume of silicon.[9] For monomers with a Si group connected to dimethyl siloxane groups (e.g., the TRIS component of LB), we considered the group contributions consisting of the PDMS groups, a terminal methyl, and a >Si< atom. Finally, in the SiGMA monomer of GA, we considered the silicone branching at the end as consisting of two PDMS groups, 1 silicon (>Si<) atom, and 3 methyl groups. See Supplemental Materials A for structures of each monomer, the estimated structures of the polymers, each group contribution method, and the details of the group contribution procedure.[7]

Polymer solubility parameters calculated by the HVK method employs the following equations,

$$\delta_{\mathrm{d}} = \frac{\sum \mathrm{F}_{\mathrm{d,i}}}{\mathrm{V}} \tag{S1}$$

$$\delta_{\mathrm{p}} = \frac{\sum \mathrm{F}_{\mathrm{p,i}}^{2}}{\mathrm{V}} \tag{S2}$$

$$\delta_{\mathrm{h}} = \sqrt{\frac{\sum \mathrm{E}_{\mathrm{h,i}}}{\mathrm{V}}} \tag{S3}$$

$$\delta_{\mathrm{t}}^{2} = \delta_{\mathrm{d}}^{2} + \delta_{\mathrm{p}}^{2} + \delta_{\mathrm{h}}^{2} \tag{S4}$$

where δ_d is the dispersive solubility parameter, δ_p is the polar solubility parameter, δ_h is the hydrogen bonding solubility parameter, δ_t is the overall average solubility parameter, and V is the molar volume. The parameters $F_{d,i}$, $F_{p,i}$ and $E_{h,i}$ are the dispersive, polar and hydrgen-bonding contributions from group i. For PDMS, we calculated polymer molar volume using the repeat unit molecular weight and its experimental amorphous density.[10] Using the molar fraction of each monomer, we weighted proportionally the mole contributions of each group to calculate the average molecular volume.

The resulting solubility parameters are reported in Table 1 of the paper.

3 Archimedes Principle to Measure Dry Lens Density

The dry density of the contact lens were required in the HVK calculations and in calculations of volumetric swelling. We could find no published densities of dry contact lens materials, so we made the measurements ourselves using the weight of a dry contact lens weight in air and the weight of the same contact lens weight in water (or other solvent). The lenses were attached to a 6 cm 32-gauge copper wire fiber using cyanoacrylate, and the fiber was attached to the bottom loading mechanism of a Mettler Toledo microbalance. The details and derivation of equations are given below. The experiments and data reduction accounted for the surface tension of the water (and other solvents) on the 6 cm 32-gauge copper wire fiber and the buoyancy of the fiber suspending the lens. This was done by using the following equations, where g is the gravitational constant, ρ is mass density, V is the volume, and W is the force of the weight measured by the balance with the lens suspended in air or water. These equations below ignore the weight of polycyanoacrylate, the weight of the copper wire, and the force (downward) of the meniscus of water on the wire. Those corrections are subsequently accounted for.

$$W_{air} = \rho_{CL_{dry}} V_{CL_{dry}} g - \rho_{air} V_{CL_{dry}} g \quad \text{(S5)}$$

$$W_{water} = \rho_{CL_{dry}} V_{CL_{dry}} g - \rho_{water} V_{CL_{dry}} g \quad \text{(S6)}$$

Subtracting Eq S6 from Eq S5, and rearranging gives:

$$V_{CL_{dry}} = \frac{(W_{air} - W_{water})}{g(\rho_{water} - \rho_{air})} = \frac{W_{air}}{g\left(\rho_{CL_{dry}} - \rho_{air}\right)} \quad \text{(S7)}$$

Rearranging Eq S7 gives:

$$\rho_{CL_{dry}} = \frac{W_{air}}{g\, V_{CL_{dry}}} + \rho_{air} = \frac{W_{air}(\rho_{water} - \rho_{air})}{(W_{air} - W_{water})} + \rho_{air} \ , \quad \text{(S8)}$$

all of which on the right-hand side are measured or calculated from ideal gas or water density.

Meniscus Force Measurement

As part of the calculation of the mass of the swollen contact lens, we had to determine the force that the water meniscus pulled downward upon the wire. We hung an ethanol-cleaned 6-cm 32-gauge copper wire from the bottom of the microbalance to measure its weight. A clean square beaker, filled with distilled-deionized water, was raised to touch the copper wire. This produced an instant increase in weight on the balance. We then measured a linear decrease of weight on the balance at immersion depths of 1 cm, 2 cm, and 3 cm, and then extrapolated these values to the 0-cm point. We repeated this experiment 15 times and averaged each experiment to calculate the meniscus force.

This meniscus force was subtracted from the measured forces W_{water} and W_{air} used in the equations above.

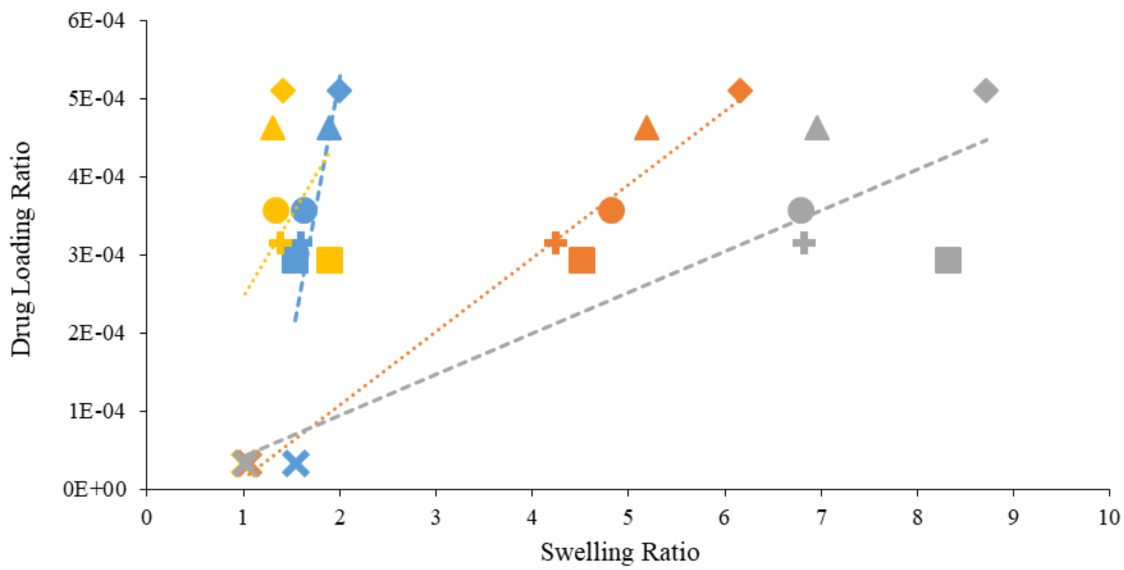
Weight of Cyanoacrylate

Some contact lenses required adhesion with a drop of cyanoacrylate, and sometimes more because not all contact lenses adhered to the wire with the first drop. To account for this, we calculated the weight of a single drop of cyanoacrylate. A clean 6-cm 32-gauge copper wire was hung from the bottom of the microbalance and weighed. We then dipped the end of the wire into the cyanoacrylate and weighed it again. We averaged 15 such measurements to estimate the drop weight.

The weight of cyanoacrylate was subtracted from the measured forces W_{water} and W_{air} used in the equations above.

4 Correlations of drug uptake and swelling ratio

The paper states that "There is a good correlation (*R*=0.979) between the amount of drug uptake and the swelling in n-propanol". The figure below shows the drug loading ratio as a function of the mass swelling of the various contact lenses in water, n-propanol, trichloroethylene, and n-hexane with their respective colors blue, orange, grey, and yellow. The best linear correlation is the data of uptake and swelling in n-propanol.

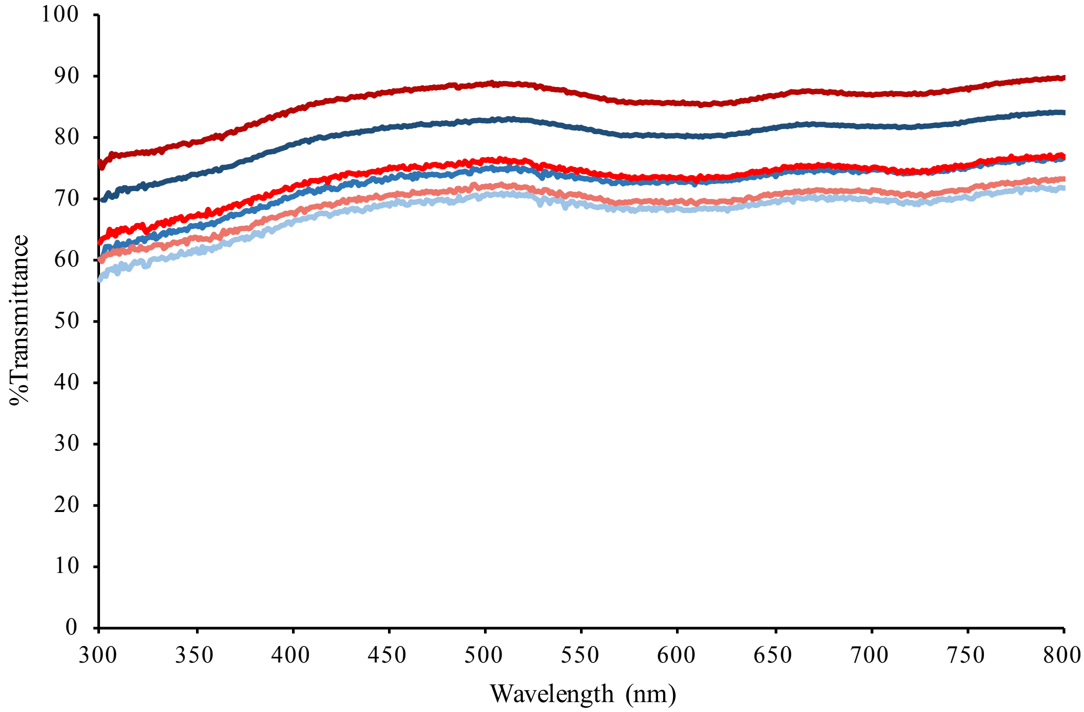


Supplemental Figure S7. The ratio of the average mass of drug uploaded in the contact lens over the average weight of the dry contact lens as a function of the ratio of the average mass of swollen contact lens over the average mass of dry contact lens in a certain solvent. The solvents are distilled-deionized water, n-propanol, trichloroethylene, and n-hexane with their respective colors blue, orange, grey, and yellow. The shapes are ●, ▲, ■, ♦, +, and X are respectively contact lenses Balafilcon A (BA), Comfilcon A (CA), Delefilcon A (DA), Galyfilcon A (GA), Lotrafilcon B (LB), and Polymacon (PM).

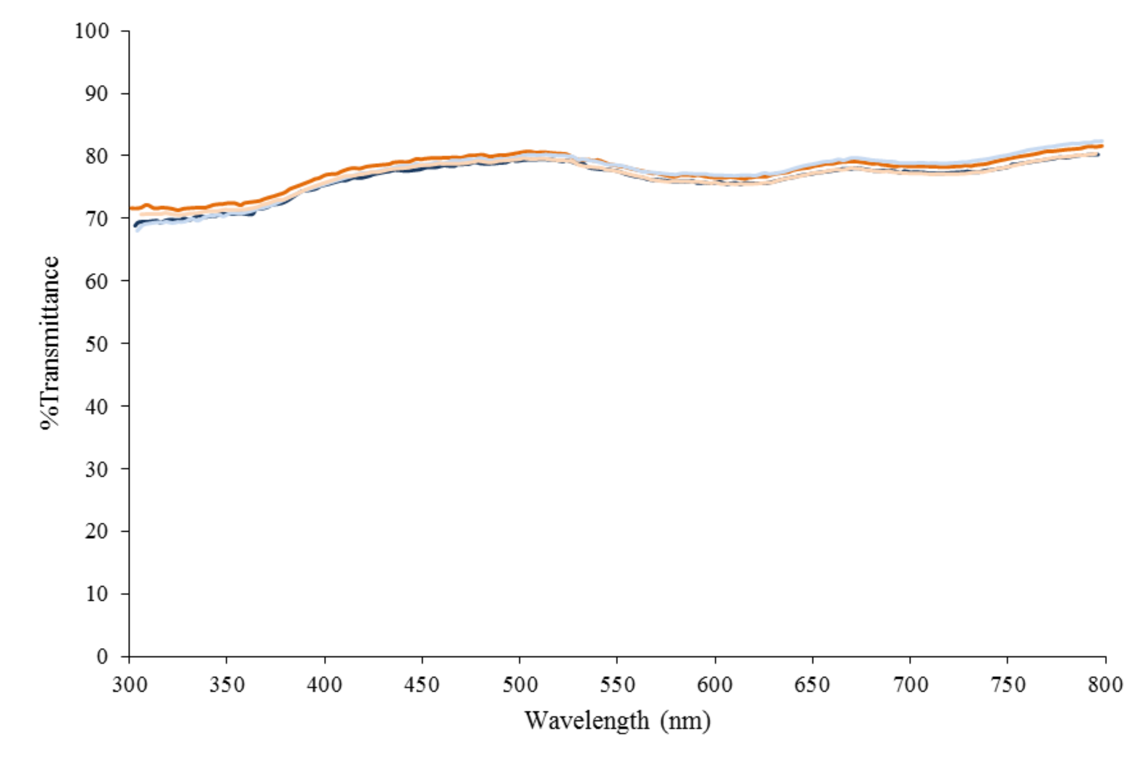
5 Calculation of estimated delivery rates from eye drops

The average dose averaged over 24 hours is 0.059 µg/hr, but is further corrected for the inefficiency of delivery to the cornea (only about 1-5%). To make a fair comparison to contact lens release rates, the calculation also factors in estimated efficiencies of 20-70% for contact lens drug delivery directly to the cornea.[11] Based on the range of possible efficiency combinations, a contact lens could give anywhere from a 4- to 70-fold increase in efficiency of drug delivery, with the most realistic scenario somewhere between these extremes, calculated as follows. For a low estimate, 0.0024 µg/hr was calculated by assuming the maximum eye-drop retention efficiency of 5% and minimum contact lens efficiency of 20%, giving only a 4-fold boost in delivery efficiency from a contact lenses. For a high estimate, 0.015 µg/hr was calculated, assuming only 1% efficiency in eye-drop retention and a higher contact lens efficiency of 70%, giving only a 70-fold boost in lens delivery efficiency.

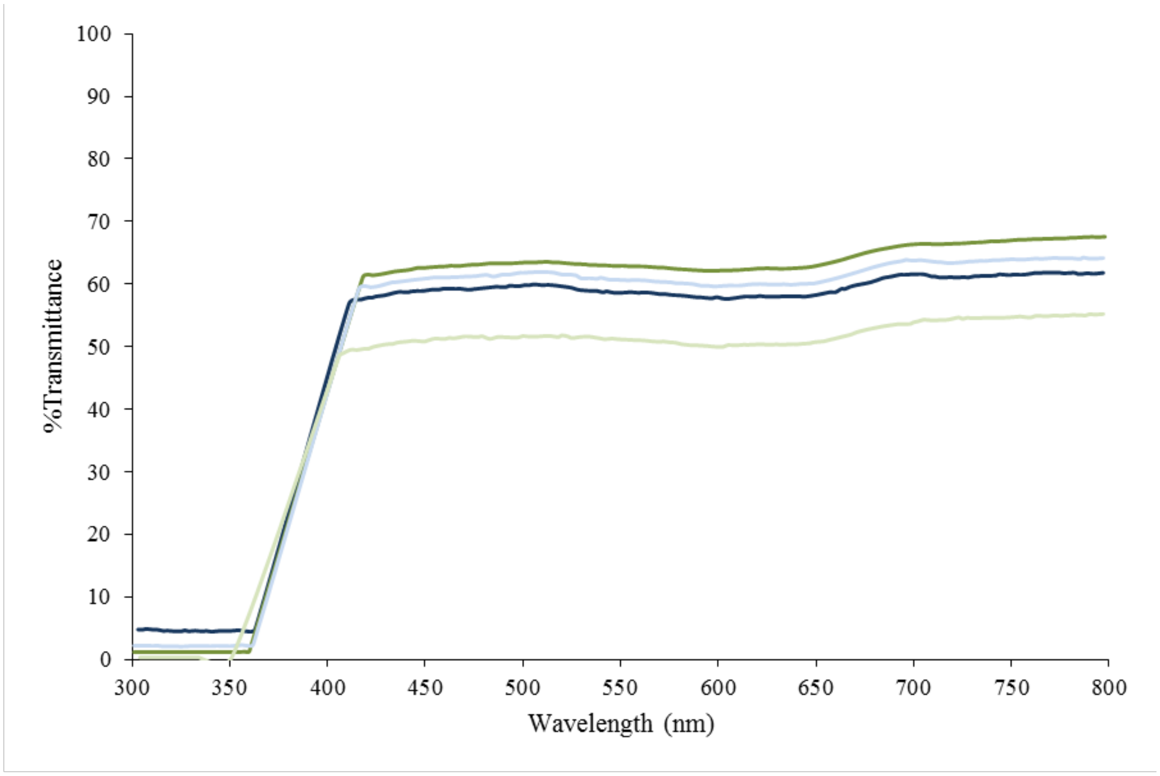
6 Transmission of visible light in fresh and latanoprost-loaded lenses



Supplemental Figure S8. The transmission of Lotrafilcon B lenses mounted on glass slides was measured before and after loading with latanoprost from a 0.125 mg/mL solution in n-propanol. The shade of the colors represents a different individual lens tested, and the blue color represents the transmission of the lens before it was loaded and the red color represents the transmission of the lens after it was loaded. There is no evidence of scattering or absorption from the latanoprost that was loaded. N = 3.



Supplemental Figure S9. The transmission of Delefilcon A lenses mounted on glass slides was measured before and after loading with latanoprost from a 0.125 mg/mL solution in n-propanol. The shade of the colors represents a different individual lens tested, and the blue color represents the transmission of the lens before it was loaded and the orange color represents the transmission of the lens after it was loaded. There is no evidence of scattering or absorption from the latanoprost that was loaded. N = 2.

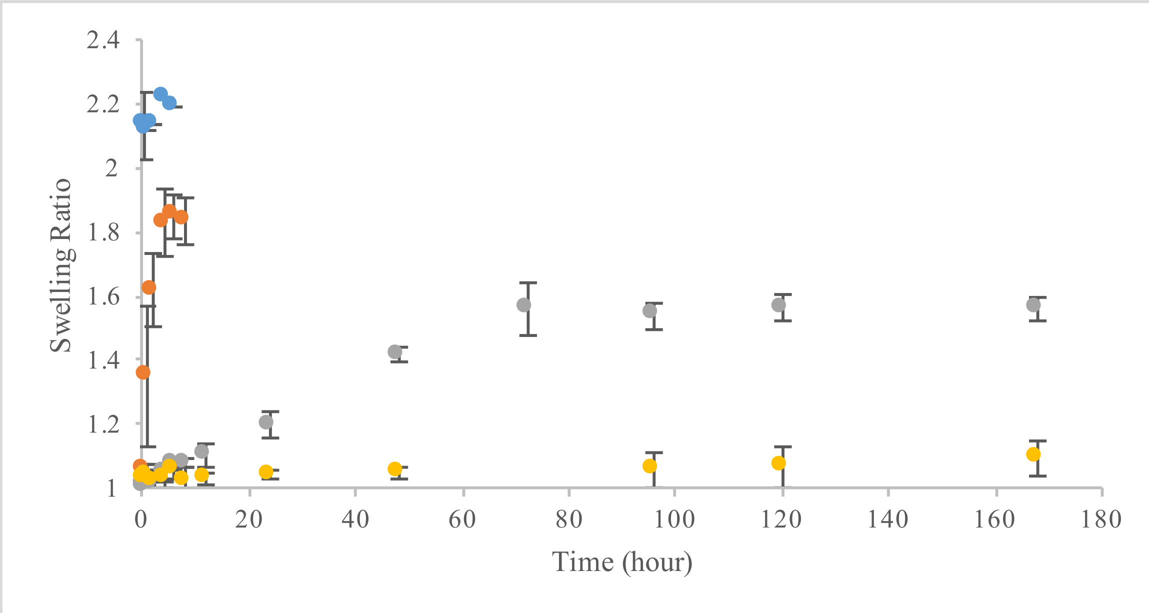


Supplemental Figure S10. The transmission of Galyfilcon A lenses mounted on glass slides was measured before and after loading with latanoprost from a 0.125 mg/mL solution in n-propanol. The shade of the colors represents a different individual lens tested, and the blue color represents the transmission of the lens before it was loaded and the green color represents the transmission of the lens after it was loaded. There is no evidence of scattering or absorption from the latanoprost that was loaded. N = 2.

7 Swelling of Polymacon Lenses in Alcohols

SofLens38 lenses were dried as desribed in the paper (section 2.2). Briefly, they were soaked in water to remove packing solution, dried, weighed, and then placed in a capped vial containing methanol, ethanol, n-propanol or n-butanol. At designated times, the lenses were removed from the alcohol, blotted with a Kimwipe™, weighed, and returned to the vial. Mass swelling is reported as the mass of the swollen contact lens divided by the original mass. The figure below (Fig S8) shows the swelling as a function of time. The rate of swelling decreases substantially as the number of methylene groups increases in this alcohol series.

In methanol, the polymacon lens achieves a mass swelling ratio of about 2.15 ± 0.06 (mean ± StDev) in less than 10 minutes. In ethanol, the swelling ratio reaches an apparent equilibrium at about 1.84 ± 0.07 in 4 hours. In n-propanol, it takes about 72 hours to reach an equilibrium swelling ratio of about 1.56 ± 0.04. In n-butanol 1t 168 hours, the swelling ratio reached 1.1 ± 0.05, and may not have been complete.



Supplemental Figure S11. The mass swelling ratio is the average of swollen masses of polymacon lenses divided by the dry masses, presented here as a function of time in various solvents. The solvents are methanol, ethanol, n-propanol, and n-butanol with their respective colors blue, orange, grey, and yellow. Further data points for methanol and ethanol were not measured after equilibrium was confirmed. The error bars represent the standard deviation (n = 3 or 4).

8 Residual n-propanol in lenses

To determine the efficiency of our procedure to remove n-propanol from the lenses, we measured the residual amount of n-propanol using gas chromatography as follows. Lenses were swelled (4 minutes) and deswelled following the procedure described in section 2.2.2. Then the lenses were extracted in 15 mL of pure water for at least 3 hours in a clean glass vial. After lens removal the sample was submitted (along with serial dilution of n-propanol standards) for gas chromatography analysis in the Food Science Department at Brigham Young University. Results showed that the n-propanol remaining in a Balafilcon A lens was 19.2 nL. The amount remaining in a Comfilcon A lens was 5.7 nL. These values are below the toxicity levels for n-propanol, which are about 170 nL/lens for fish cells[12] and about 514 nL/lens for Hep G2 cells.[13]

8 Supplemental References

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