Supporting Information

Evaluation of Polymer-Preservative Interactions for Preservation Efficacy: Molecular Dynamics Simulation and QSAR Approaches

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S1. Molecular simulation

Table S1. Molecular models of polymers in terms of polymer chains and monomers.

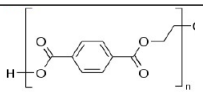
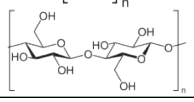
Polymer	Structure	Number of chains	Number of monomers	Total monomers	Monomer molecular weight (g/mol)	Total mass (g)
PET		18	25	450	192	86400
PP		18	114	2052	42	86348
Cellulose		18	30	540	162	87555

Table S2. 7-step compression and relaxation scheme.[1]

Step	Description	Duration (ps)
1	Energy minimization at 0 K	10
2	NPT MD simulation at 293 K and 3000 bar	300
3	NVT MD simulation at 800 K	100
4	NVT MD simulation at 293 K	100
5	NPT MD simulation at 293 K and 1000 bar	300
6	Repeat Step (3)-(5) for 29 times	
7	NPT MD simulation at 293 K and 1 bar	10000

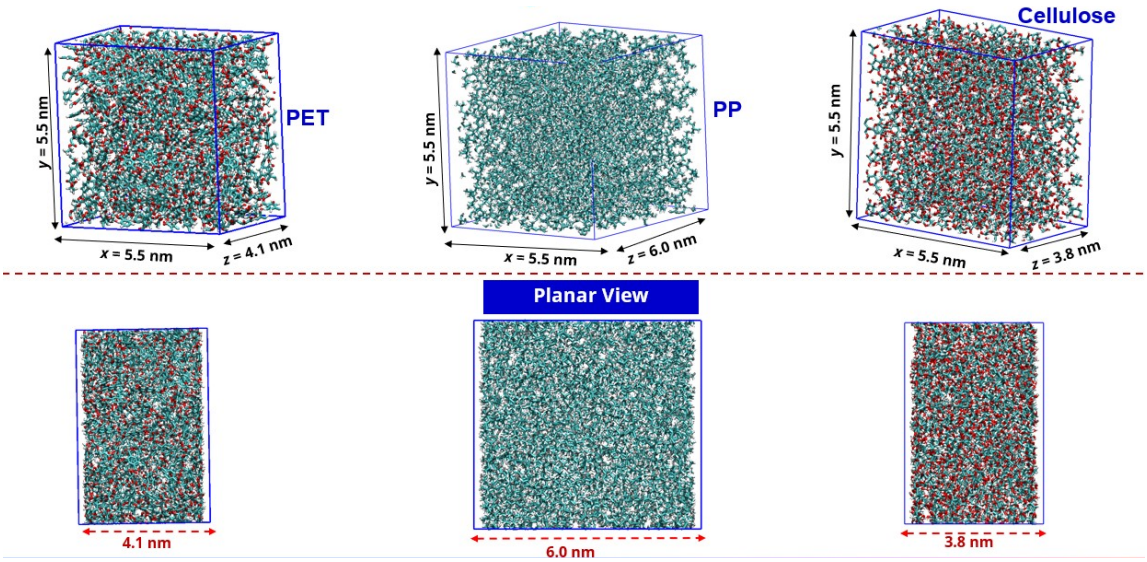


Figure S1. Polymer models for adsorption simulation.

Table S3. List of preservatives with pKa values, number of neutral and ionic forms.

Entry	Preservatives	pKa	Number of neutral forms	Number of ionic forms
1	Hexanediol	14.5	10	0
2	Octanediol	14.6	10	0
3	Glyceryl caprylate	-	10	0
4	Ethylhexylglycerin	13.7	10	0
5	Sorbitan caprylate	-	10	0
6	Benzyl alcohol	15.4	10	0
7	Phenethyl alcohol	15.88	10	0
8	Phenylpropanol	15.96	10	0
9	Hydroxyacetophenone	9.15	10	0
10	Phenoxyethanol	15.10	10	0
11	Levulinic acid	4.65	8	2
12	Succinic acid	4.61 and 5.61	8	2
13	Citric acid	3.1, 4.7 and 6.4	8	1 ($C_6H_7O_7^-$) and 1 ($C_6H_6O_7^{2-}$)
14	Benzoic acid	4.2	7	3
15	*p*-Anisic acid	4.47	8	2

S2. QSAR modelling

Table S4. 22 uncorrelated descriptors of preservatives for QSAR modelling.

1	Molecular_Solubility	12	Jurs_PPSA_3
2	ALogP	13	Jurs_FPSA_3
3	Molecular_Volume	14	Jurs_RPCG
4	Molecular_PolarSurfaceArea	15	Shadow_YZ
5	Dipole_mag	16	Shadow_XYfrac
6	Kappa_3	17	Shadow_XZfrac
7	SC_3_C	18	Shadow_YZfrac
8	IC	19	Shadow_nu
9	BIC	20	Shadow_Ylength
10	CIC	21	Shadow_Zlength
11	IAC_Mean	22	JX

All QSAR modelling and sensitivity analysis were performed using the *scikit-learn*[2] and *scikit-optimize*[3] packages. Specifically, *RandomForestRegressor*, *RFE*, *r2_score* and *mean_squared_error* objects in *scikit-learn* package were utilized for random forest (RF), recursive feature elimination (RFE), coefficient of determination (R^2) and root-mean-squared error (RMSE), respectively. The *BayesSearchCV* object in *scikit-optimize* package was used to tune the hyperparameters of RF, where **Table S5** lists the range of explored hyperparameters.

Table S5. Range of hyperparameters explored for random forest.

Hyperparameters	Range of values explored
n_estimators	[50 to 1000]
max_depth	[‘None’, 1 to 5]
min_samples_split	[2 to 5]
min_samples_leaf	[1 to 5]

S3. Simulation results

Table S6. PET density at 293 K as a function of number of polymer chains and monomers.

Simulation system	Run 1	Run 2	Run 3	Average density (g/cm^3)
3 chains of 150 monomers	1.254	1.258	1.260	1.258 ± 0.003
6 chains of 75 monomers	1.254	1.263	1.264	1.260 ± 0.006
18 chains of 25 monomers	1.259	1.258	1.252	1.260 ± 0.004

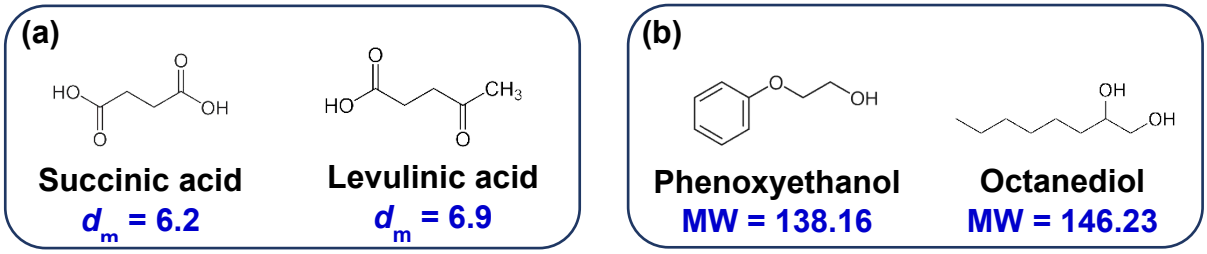


Figure S2. Chemical structures, sizes, and molecular weights for (a) organic acid and (b) alcohol preservative.

S4. QSAR model results

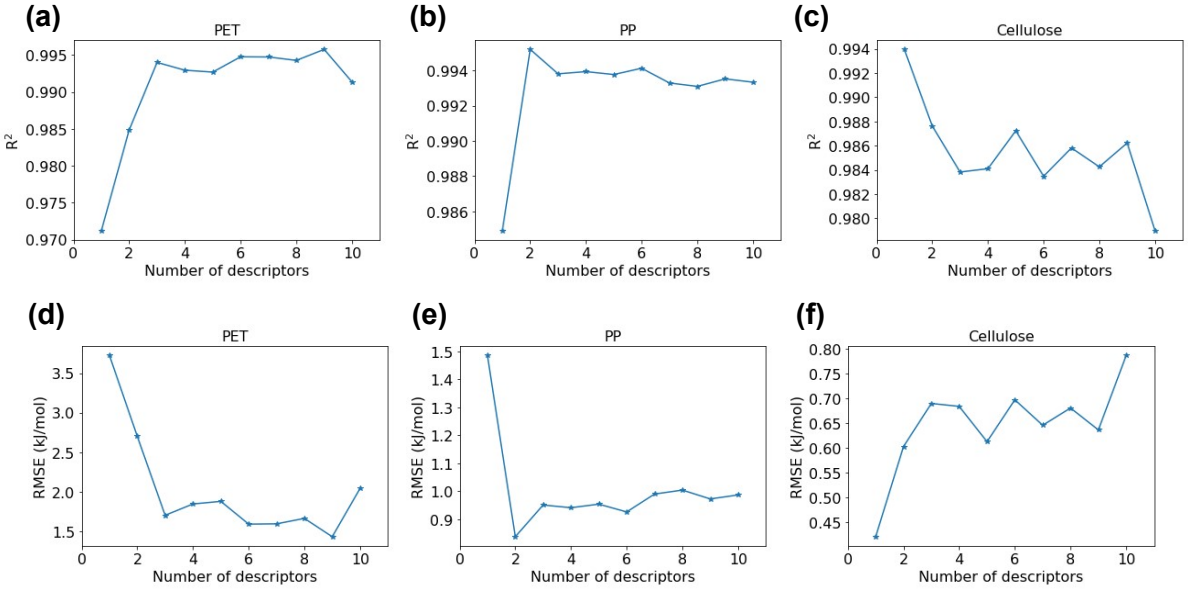


Figure S3. Sensitivity analysis of (**T1**) IEs between preservatives and polymers at interface for various polymers in terms of (a)-(c) R^2 and (d)-(f) RMSE.

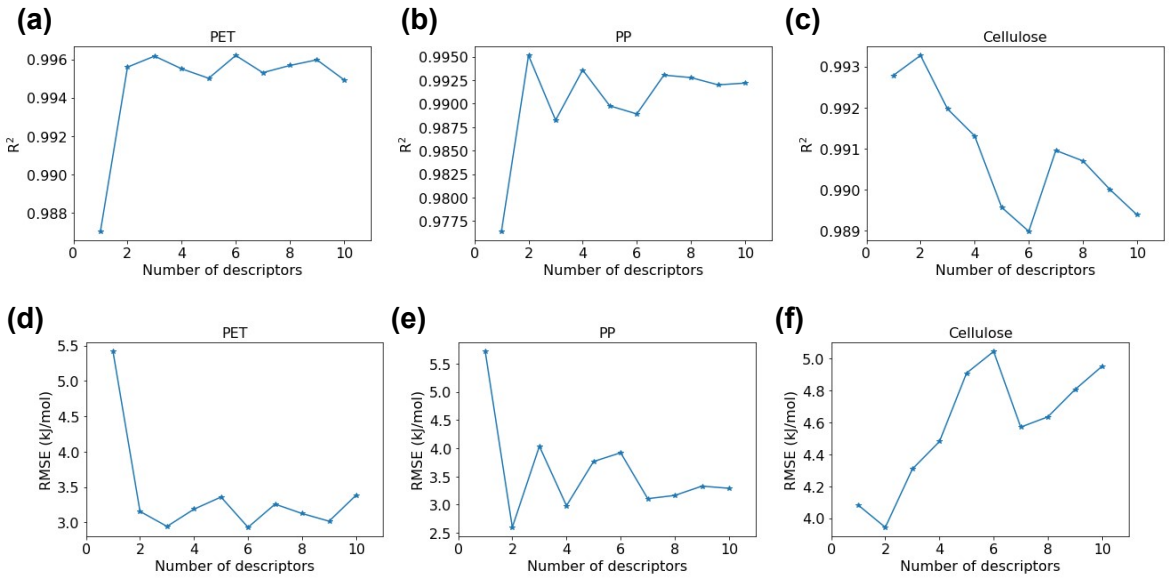


Figure S4. Sensitivity analysis of (**T2**) IEs between preservatives and water for various polymers in terms of (a)-(c) R^2 and (d)-(f) RMSE.

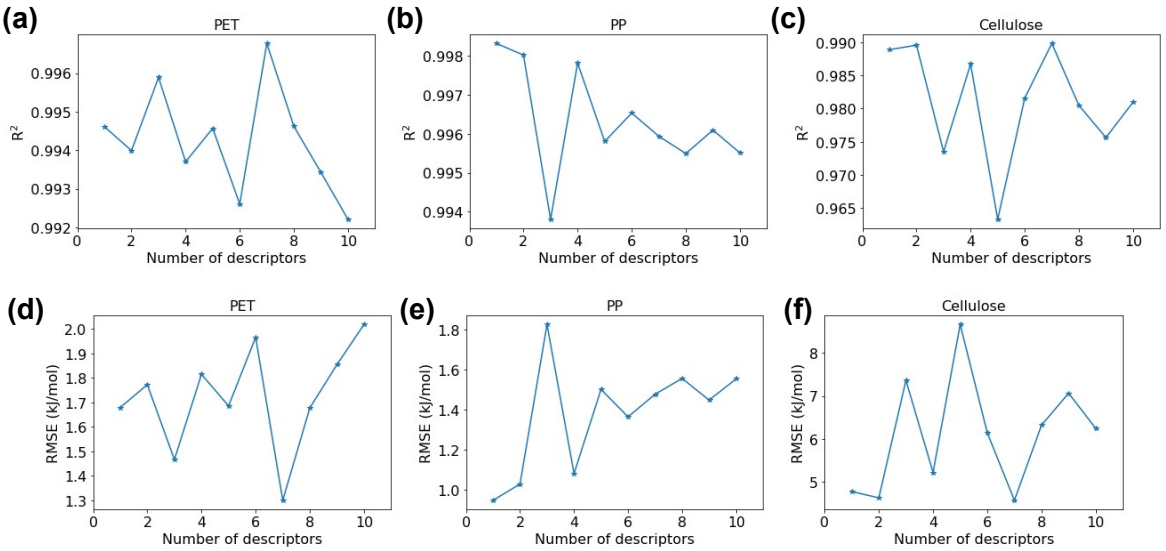


Figure S5. Sensitivity analysis of (**T3**) interior IE between preservatives and polymers for various polymers in terms of (a)-(c) R^2 and (d)-(f) RMSE.

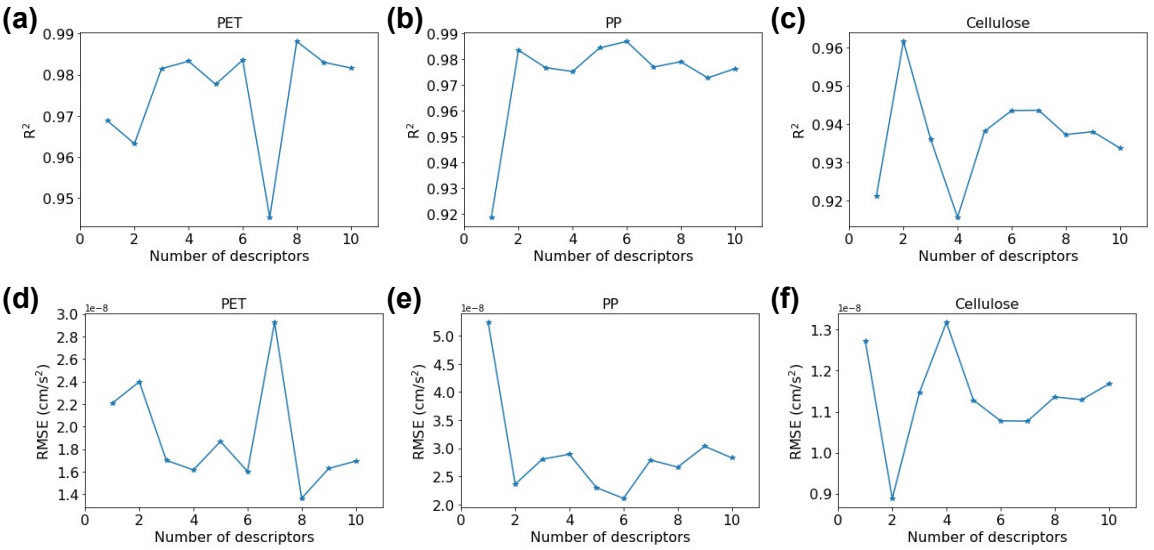


Figure S6. Sensitivity analysis of (**T4**) diffusion coefficients of preservatives in polymers in terms of (a)-(c) R^2 and (d)-(f) RMSE.

References

1. Shi, Q.; Zhang, K.; Lu, R.; Jiang, J., Water desalination and biofuel dehydration through a thin membrane of polymer of intrinsic microporosity: Atomistic simulation study. *J. Membr. Sci.* **2018,** *545*, 49-56.
2. Pedregosa, F.; Varoquaux, G.; Gramfort, A.; Michel, V.; Thirion, B.; Grisel, O.; Blondel, M.; Prettenhofer, P.; Weiss, R.; Dubourg, V., Scikit-learn: Machine learning in Python. *J. Mach. Learn. Res.* **2011,** *12*, 2825-2830.
3. Head, T.; MechCoder, G. L.; Shcherbatyi, I. J. V. v., scikit-optimize/scikit-optimize: v0. 5.2. **2018,** *5*.