

Molecular Docking Assessment of Tarragon Essential-Oil Constituents toward OATP1B1 and OATP1B3

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Supplementary material

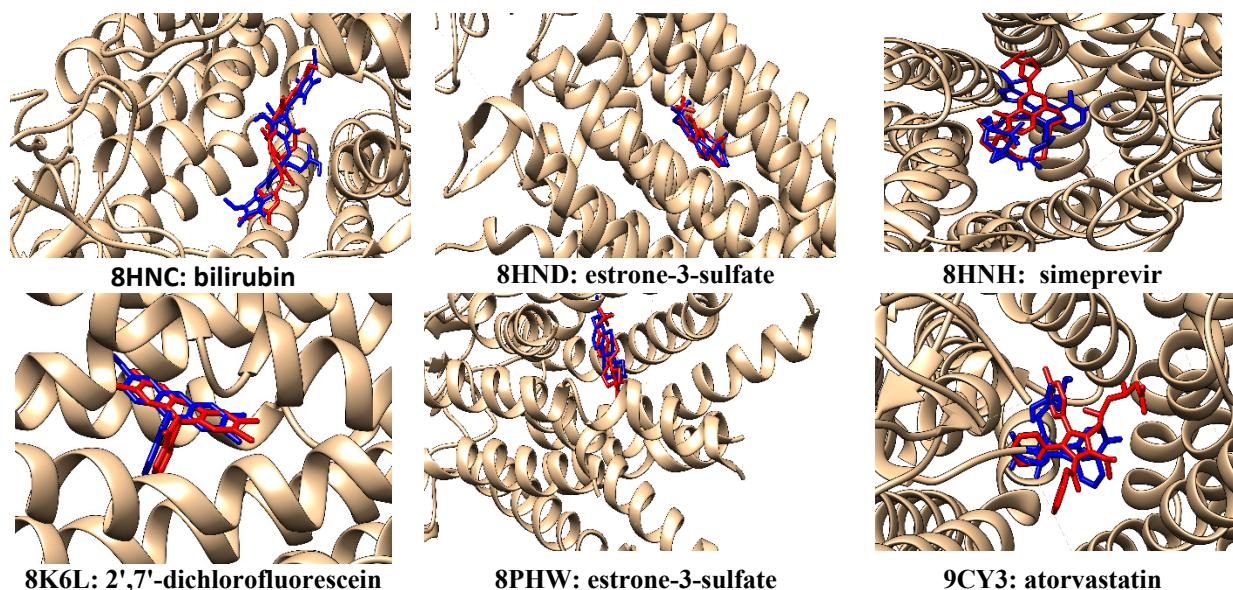


Figure S1. Comparison of the binding modes of ligands present in the PDB structures (red sticks) and re-docked ligands present in the PDB structures (blue sticks)

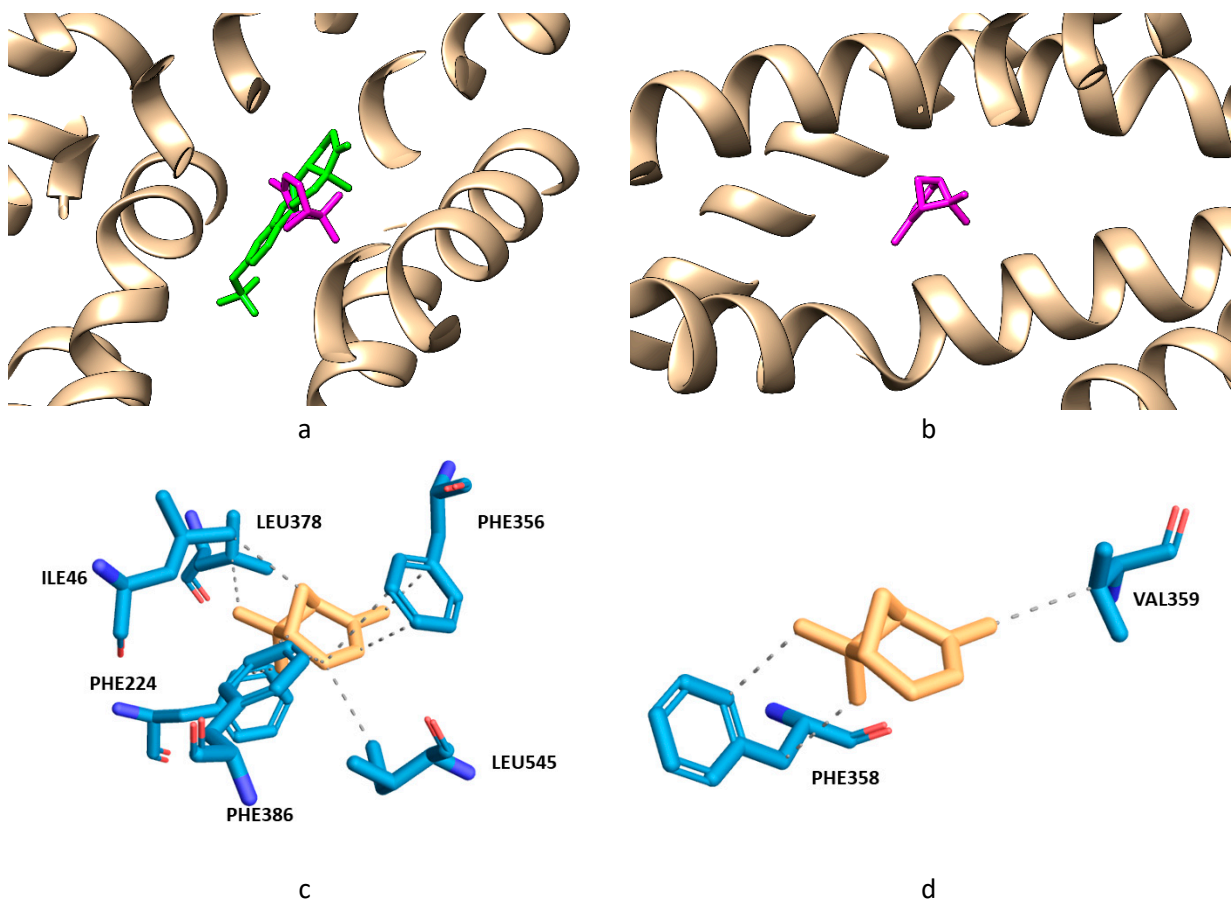
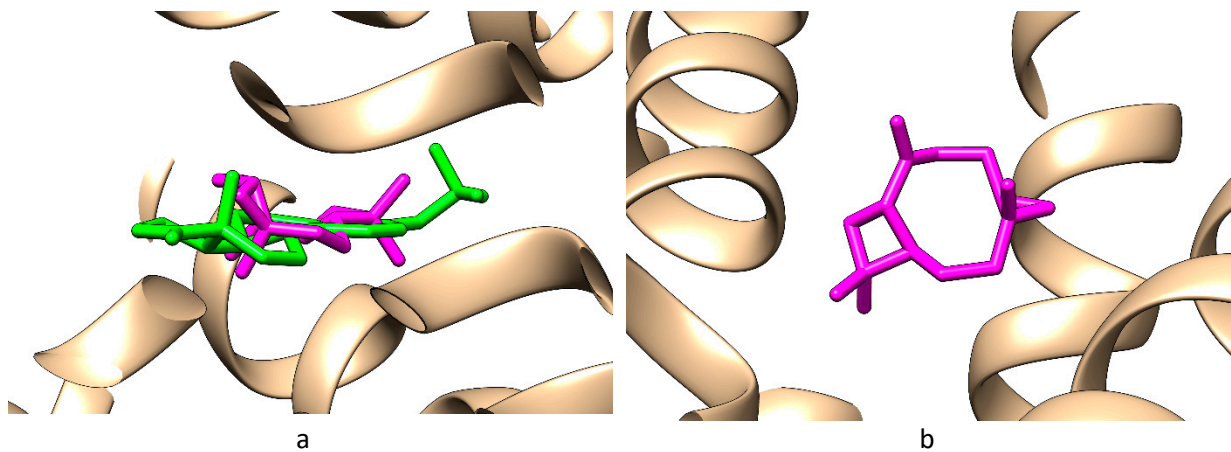


Figure S2. Best binding pose of α -pinene (magenta sticks) in OATP1B1 based on the PDB structure 8PHW, containing the endogenous metabolite estrone-3-sulfate (green sticks) (a), and in OATP1B3 based on the PDB structure 8PG0 (b). Corresponding OATP1B1- α -pinene (c) and OATP1B3- α -pinene (d) interaction profiles were generated using PLIP.



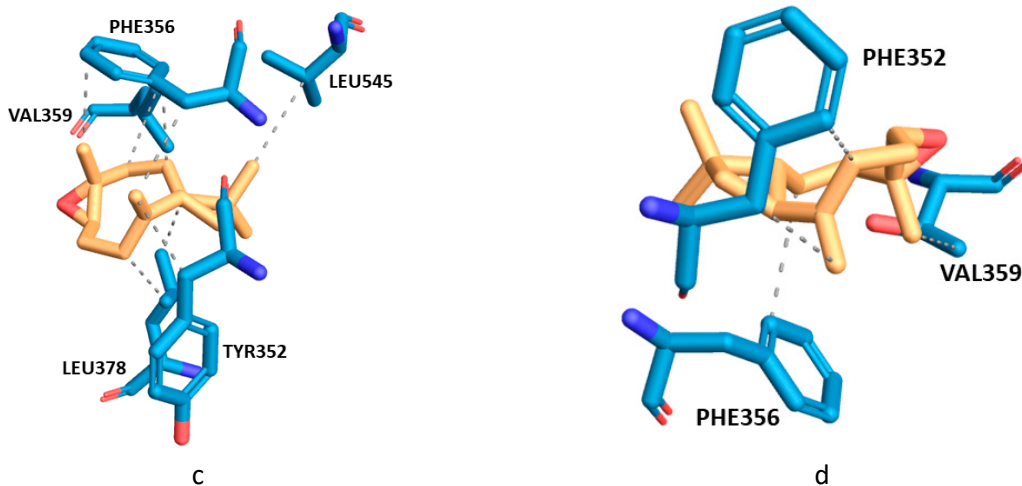


Figure S3. Best binding pose of caryophyllene oxide (magenta sticks) in OATP1B1 based on the PDB structure 8HND, containing the endogenous metabolite estrone-3-sulfate (green sticks) (a), and in OATP1B3 based on the PDB structure 8PG0 (b). Corresponding OATP1B1– caryophyllene oxide (c) and OATP1B3– caryophyllene oxide (d) interaction profiles were generated using PLIP.

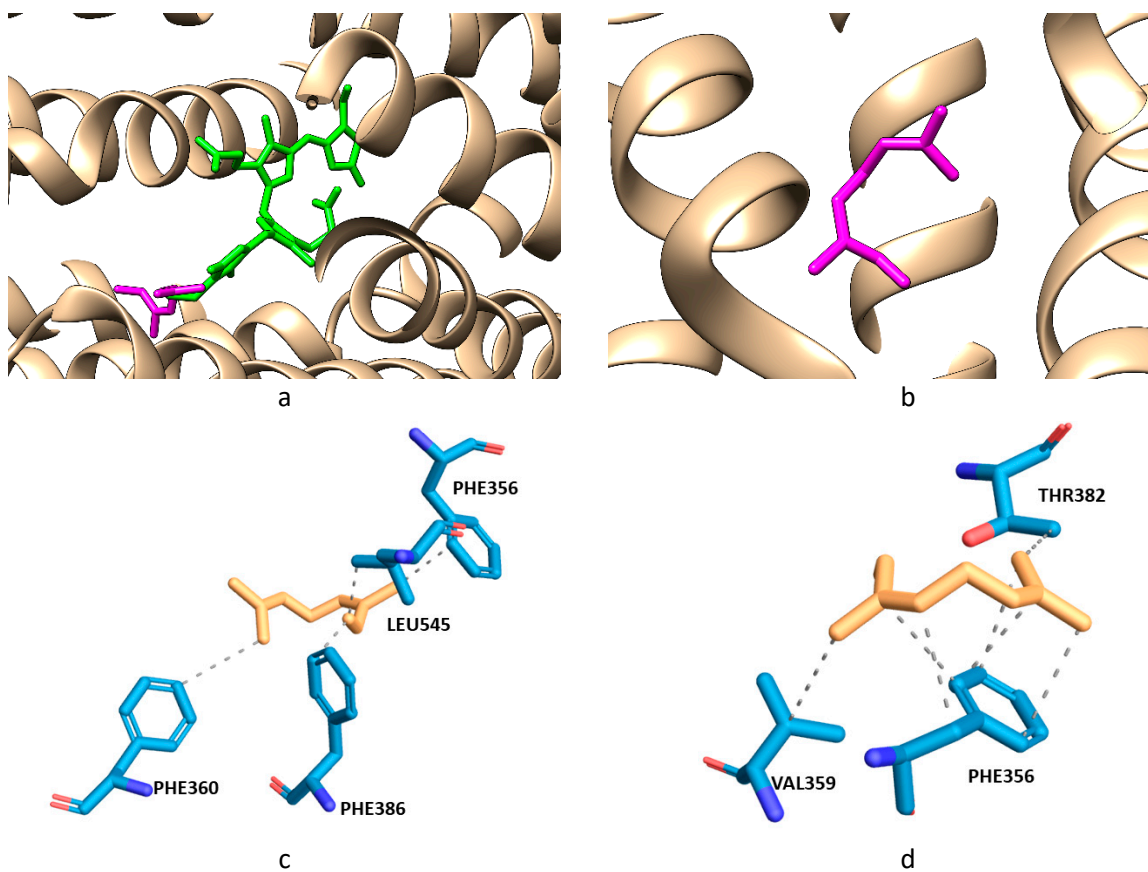


Figure S4. Best binding pose of cis- β -ocimene (magenta sticks) in OATP1B1 based on the PDB structure 8HNC, containing the endogenous metabolite bilirubin (green sticks) (a), and in OATP1B3 based on the PDB structure 8PG0 (b).

(b). Corresponding OATP1B1– cis- β -ocimene (c) and OATP1B3– cis- β -ocimene (d) interaction profiles were generated using PLIP.

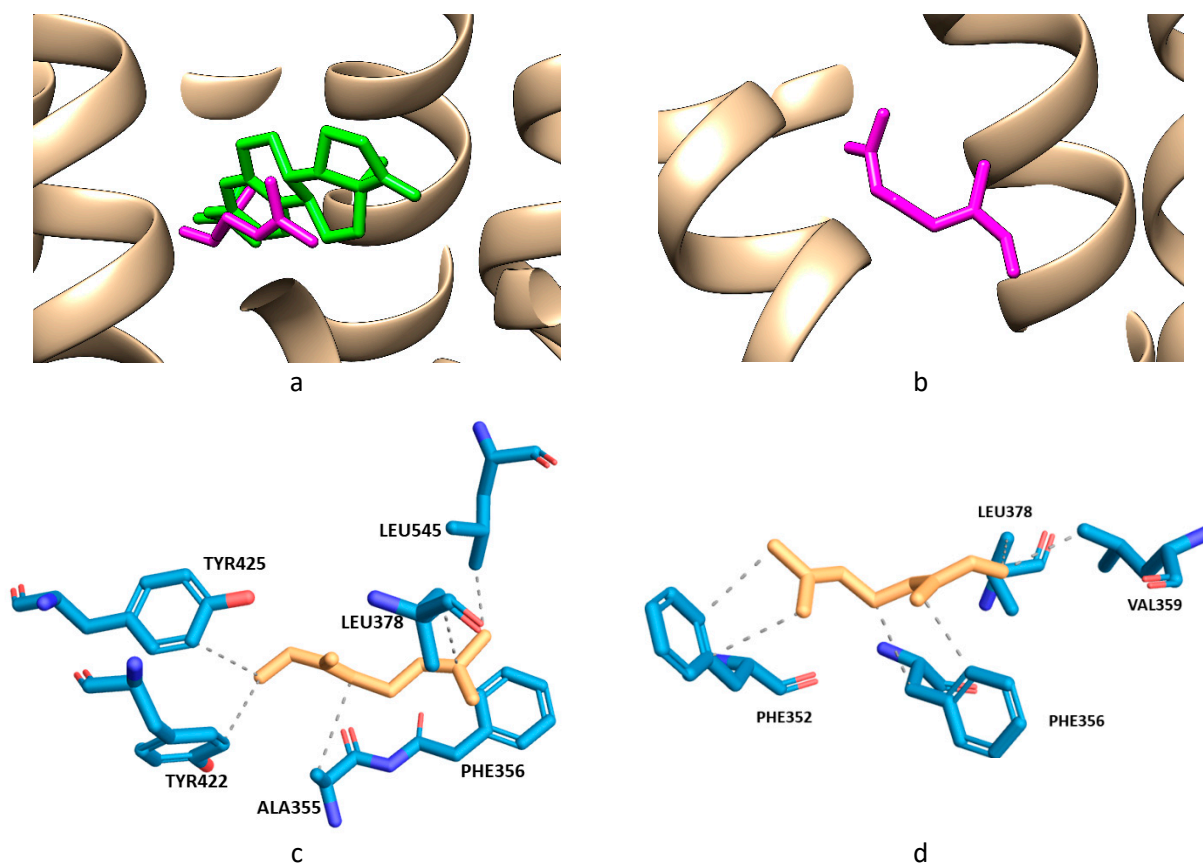
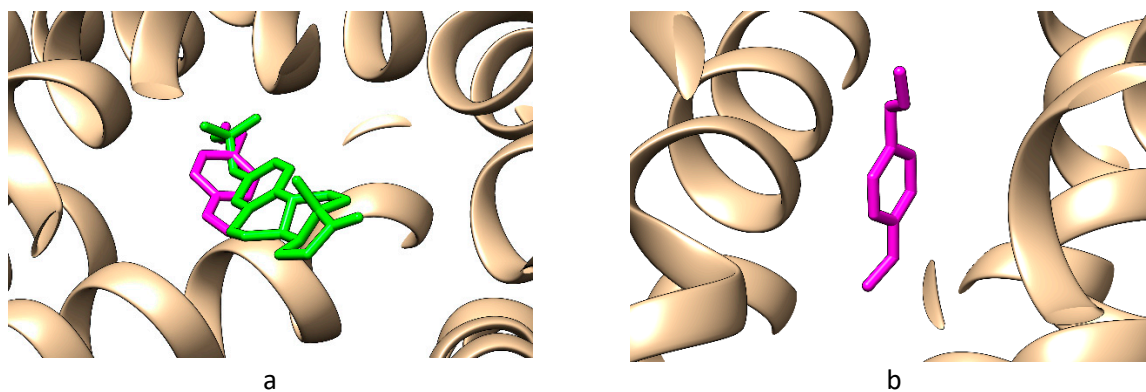


Figure S5. Best binding pose of trans- β -ocimene (magenta sticks) in OATP1B1 based on the PDB structure 8HND, containing the endogenous metabolite estrone-3-sulfate (green sticks) (a), and in OATP1B3 based on the PDB structure 8PG0 (b). Corresponding OATP1B1– trans- β -ocimene (c) and OATP1B3– trans- β -ocimene (d) interaction profiles were generated using PLIP.



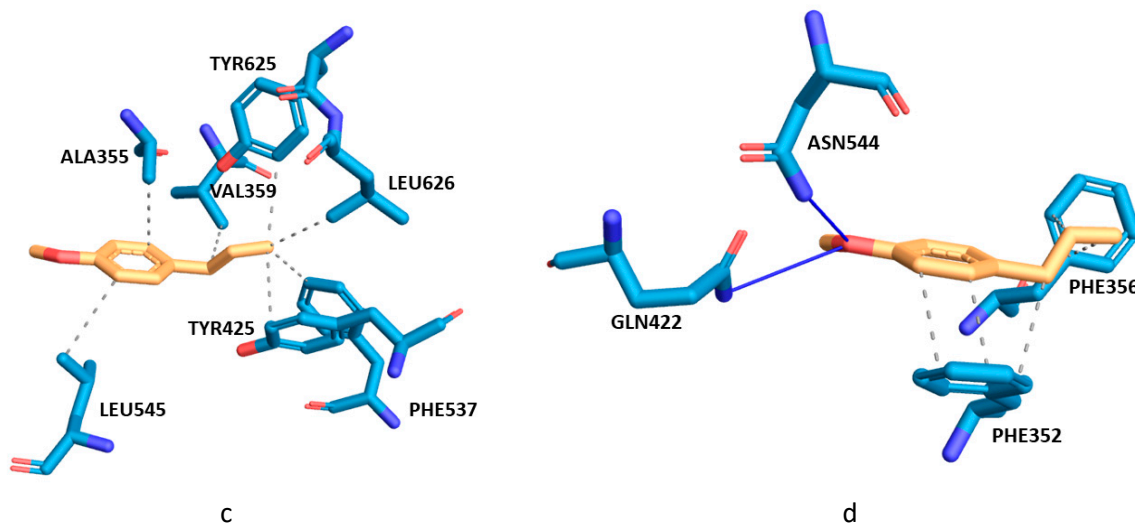


Figure S6. Best binding pose of estragole (magenta sticks) in OATP1B1 based on the PDB structure 8HND, containing the endogenous metabolite estrone-3-sulfate (green sticks) (a), and in OATP1B3 based on the PDB structure 8PG0 (b). Corresponding OATP1B1– estragole (c) and OATP1B3– estragole (d) interaction profiles were generated using PLIP.

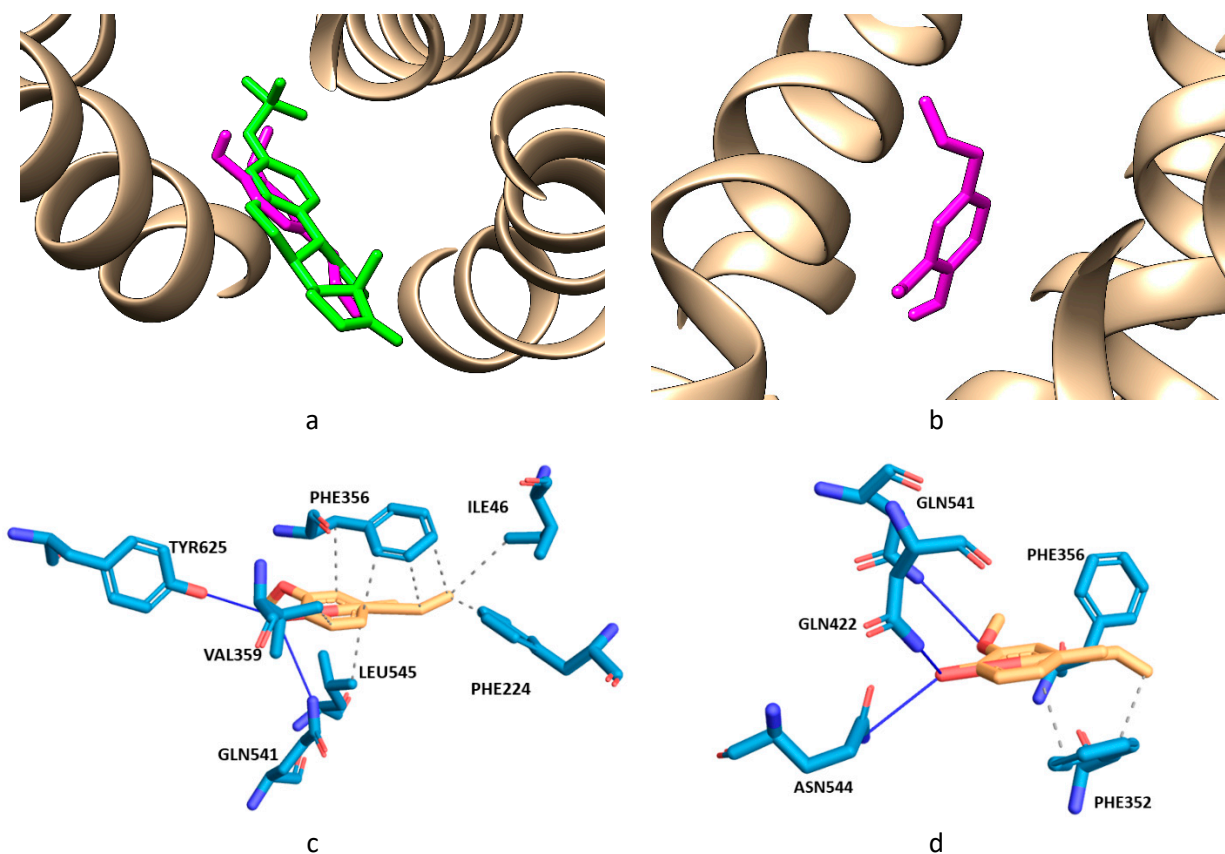


Figure S7. Best binding pose of eugenol (magenta sticks) in OATP1B1 based on the PDB structure 8HND, containing the endogenous metabolite estrone-3-sulfate (green sticks) (a), and in OATP1B3 based on the PDB structure 8PG0 (b). Corresponding OATP1B1– eugenol (c) and OATP1B3– eugenol (d) interaction profiles were generated using PLIP.

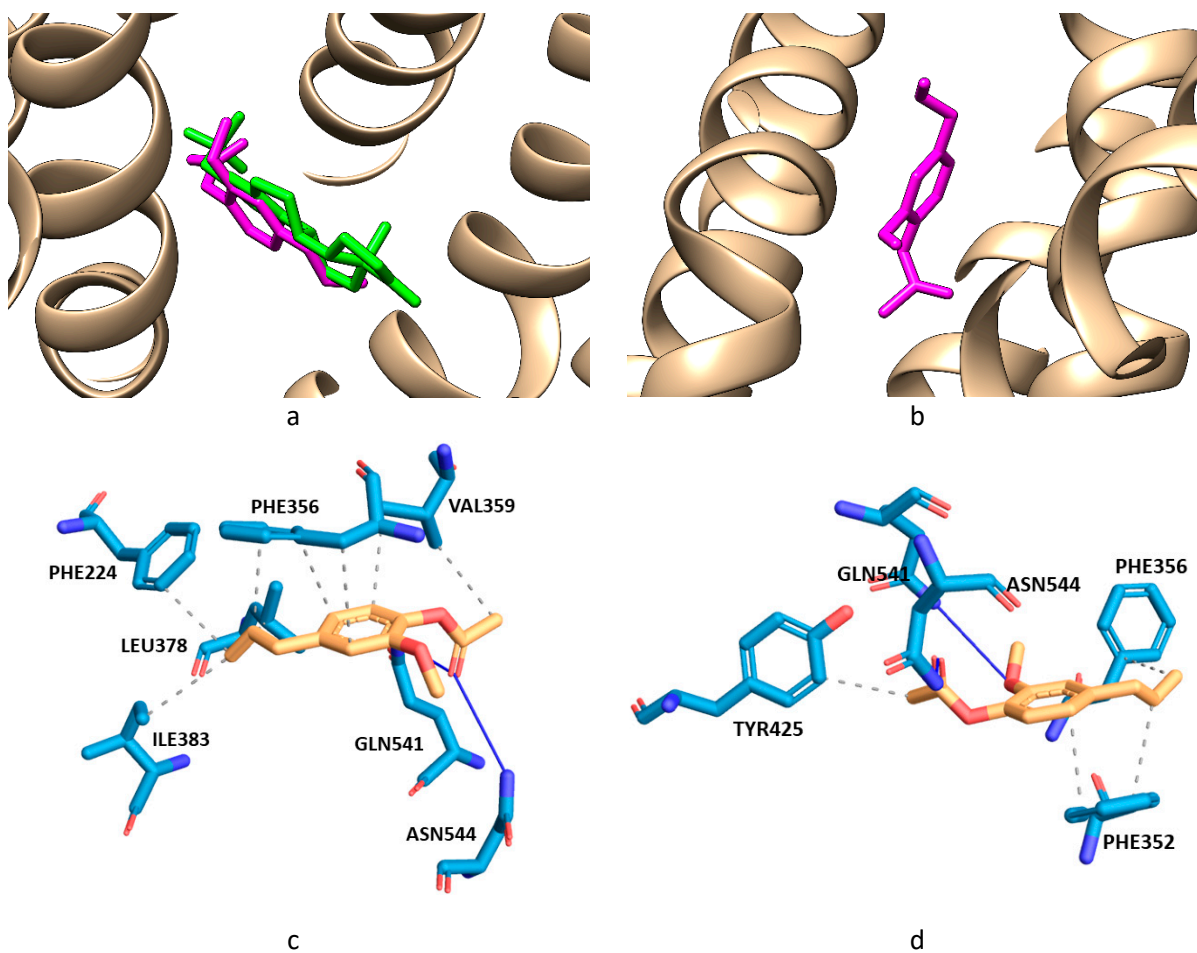
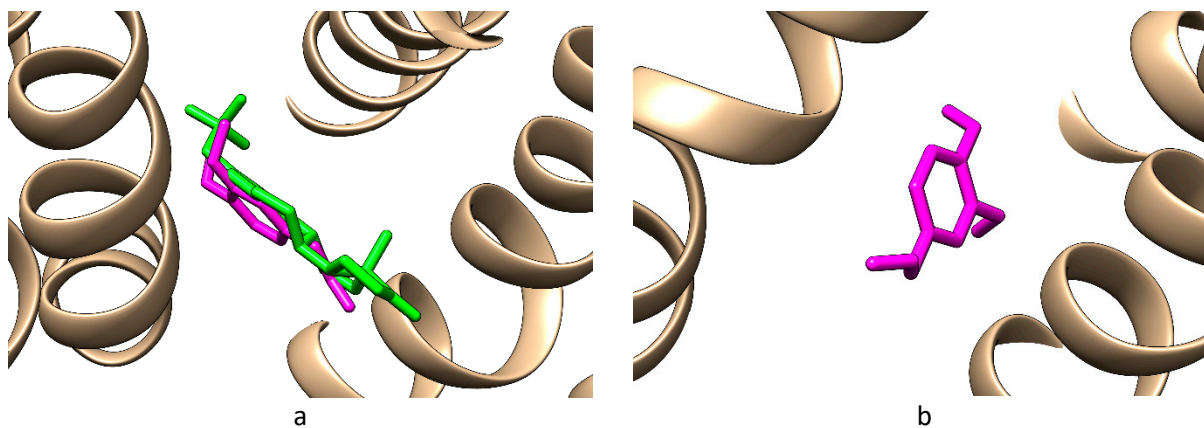


Figure S8. Best binding pose of eugenol acetate (magenta sticks) in OATP1B1 based on the PDB structure 8HND, containing the endogenous metabolite estrone-3-sulfate (green sticks) (a), and in OATP1B3 based on the PDB structure 8PG0 (b). Corresponding OATP1B1– eugenol acetate (c) and OATP1B3 – eugenol acetate (d) interaction profiles were generated using PLIP.



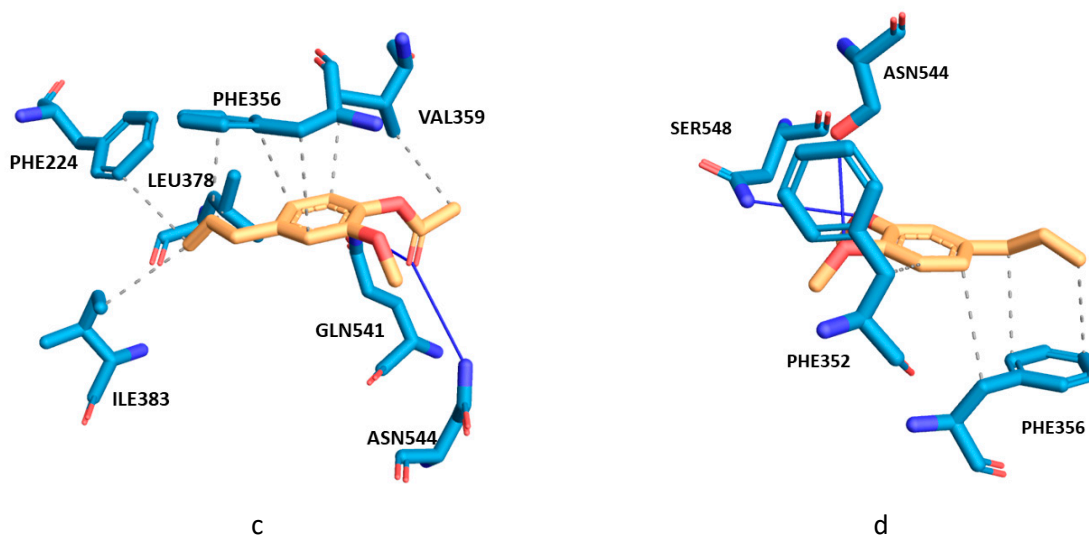


Figure S9. Best binding pose of eugenol methyl ether (magenta sticks) in OATP1B1 based on the PDB structure 8HND, containing the endogenous metabolite estrone-3-sulfate (green sticks) (a), and in OATP1B3 based on the PDB structure 8PG0 (b). Corresponding OATP1B1– eugenol methyl ether (c) and OATP1B3 – eugenol methyl ether (d) interaction profiles were generated using PLIP.

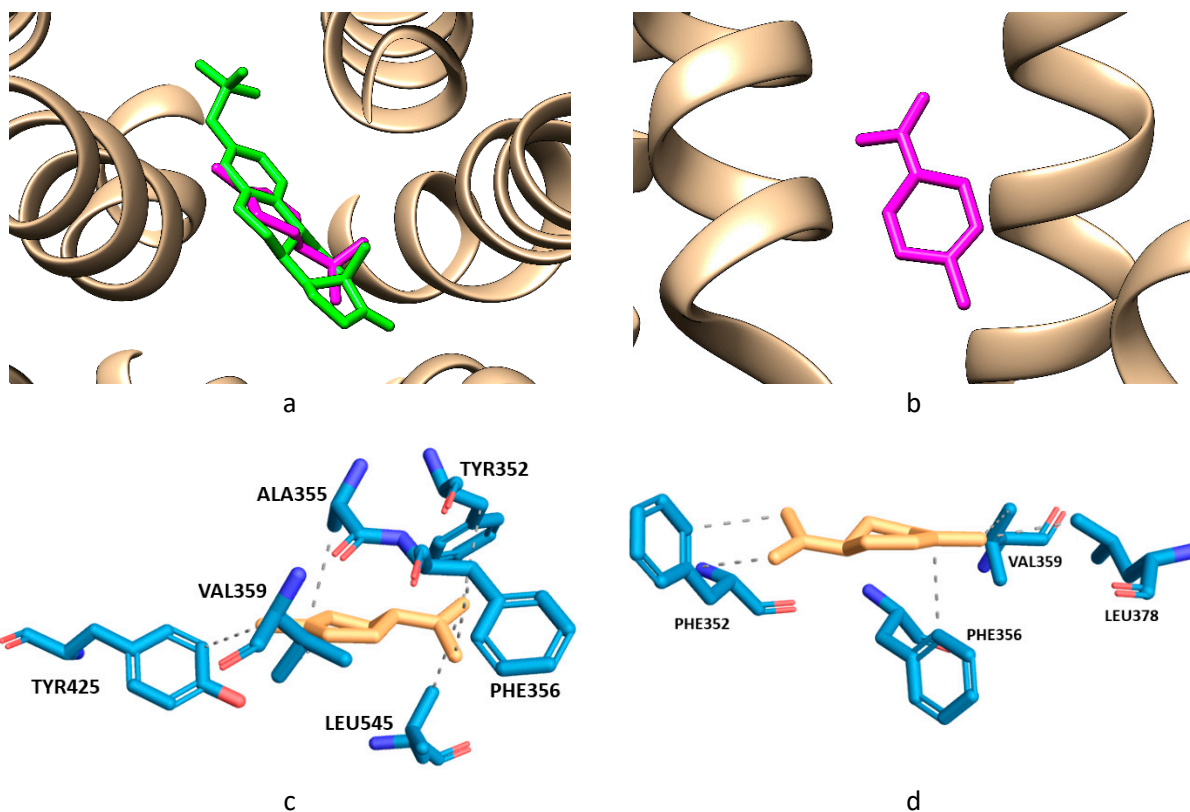


Figure S10. Best binding pose of limonene (magenta sticks) in OATP1B1 based on the PDB structure 8HND, containing the endogenous metabolite estrone-3-sulfate (green sticks) (a), and in OATP1B3 based on the PDB

structure 8PG0 (b). Corresponding OATP1B1– limonene (c) and OATP1B3 – limonene (d) interaction profiles were generated using PLIP.

Supplementary Table S1. The reported percentages of investigated constituents of tarragon essential oils found on Romanian market: eot-c—commercial tarragon essential oil, eot-mw—essential oil obtained after microwave hexane extraction of shredded dried tarragon (Pujicic, A.; Popescu, I.; Dascalu, D.; Petreuş, D.E.; , Isvoran, A. Predictions of the Biological Effects of the Main Components of Tarragon Essential Oil. International Journal of Molecular Sciences 2025, 26, 1860. doi: 10.3390/ijms26051860)

Compound	eot-c %	eot-mw %
α -pinene	1.002	0.417
caryophyllene oxide	-	2.473
cis- β -ocimene	8.422	1.740
estragole	79.425	80.096
eugenol	-	1.977
eugenol acetate	-	2.048
eugenol methyl ether	0.378	4.028
limonene	3.135	2.376
trans- β -ocimene	6.690	2.299

Supplementary Table S2. The box centers and box dimensions used for docking for each PDB structure and RMSD values between experimental and re-docked ligand poses for each structure

PDB structure	Cartesian coordinates (x; y; z) of the box center (Å)	Box dimensions (Å ³)	RMSD (Å)
8HNB	105.0; 113.0; 109.0	27x30x30	-
8HNC	108.0; 107.0; 105.0	20x25x52	6.836
8HND	104.0; 104.0; 102.0	25x33x27	3.617
8HNH	105.0; 113.0; 109.0	27x30x30	4.612
8K6L	120.0; 120.0; 120.0	30x30x30	4.279
9CY1	130.0; 132.0; 126.0	30x30x30	-
9CY3	134.0; 133.0; 139.0	30x30x30	4.338
9CY4	132.0; 131.0; 128.0	30x30x30	-
8PHW	125.0; 134.0; 112.0	30x30x30	4.011
8PG0	122.0; 133.0; 111.0	30x30x30	-

Supplementary Table S3. Interactions between the compounds found in tarragon essential oil and OATP1B1 based on the PDB structure 8HNB. Numbers in parentheses indicate how many interactions occur for each amino acid.

8HNB	Hydrophobic interactions
α -pinene	PHE356, PHE386 (2), LEU545
cis- β -ocimene	PHE360, LEU378, THR382 (2), PHE386, LEU545
trans- β -ocimene	TYR352, PHE356, VAL359 (2), PHE360, LEU378 (2), PHE386, LEU545 (2)
caryophyllene oxide	PHE356, PHE360, PHE386
eugenol	PHE356 (2), PHE360, LEU378, THR382, LEU545 (2)
eugenol acetate	PHE356 (2), VAL359, LEU378, THR382, PHE386 (2), GLN541, LEU545
eugenol methyl ether	PHE356, THR382, PHE386, LEU545
estragole	PHE356, THR382, PHE386, LEU545

limonene	TYR352, PHE356 (2), VAL359 (3), PHE360 (2), LEU378 (2), LEU545 (2)
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Supplementary Table S4. Interactions between the compounds found in tarragon essential oil and OATP1B1 based on the PDB structure 8HNC. Numbers in parentheses indicate how many interactions occur for each amino acid.

8HNC	Hydrophobic interactions	H bonds
bilirubin – the ligand present in the PDB structure	TYR352, ILE353 (3), PHE356 (2), PHE360, LEU378, THR382, PHE386, ILE579	TYR352
re-docked bilirubin	TYR352, ILE353 (2), PHE356, PHE360, PHE386 (2), LEU545, ILE579, ARG580	THR357
α -pinene	PHE356, PHE386 (2), LEU545	
cis- β -ocimene	TYR352, ILE353 (3), PHE356(2), PHE360, LEU378, THR382, PHE386, ILE579	TYR352
trans- β -ocimene	PHE356 (2), VAL359, LEU378, THR382, LEU545	
caryophyllene oxide	PHE224, PHE356, ILE383, LEU545	
eugenol	PHE356, THR382, PHE386, LEU545	
eugenol acetate	PHE224, PHE356, VAL359, LEU378, THR382, ILE383, GLN541	
eugenol methyl ether	PHE356, THR382, PHE386 (3), LEU545	
estragole	PHE356, THR382, ILE383, PHE386 (3), LEU545	
limonene	PHE356, THR382, ILE383, PHE386	

Supplementary Table S5. Interactions between the compounds found in tarragon essential oil and OATP1B1 based on the PDB structure 8HND. Numbers in parentheses indicate how many interactions occur for each amino acid.

8HND	Hydrophobic interactions	H bonds
estrone-3 sulfate the ligand present in the PDB structure	PHE224, PHE356 (3), LEU378, ILE383, PHE386, LEU545	TYR422, GLN541, ASN544, TYR625
re-docked estrone-3 sulfate	ALA355, PHE356 (3), VAL359, LEU378, ILE383, PHE386 (3), LEU545	GLN541, ASN544, TYR625
α -pinene	PRO220, PHE224 (2), PHE356 (2), LEU378, ILE383, PHE386 (2), LEU545	
cis- β -ocimene	ILE46, PHE224, PHE356 (3), VAL359, LEU378 (2), THR382, LEU545	
trans- β -ocimene	ALA355, PHE356, LEU378, TYR422, TYR425, LEU545	
caryophyllene oxide	TYR352, PHE356 (3), VAL359, LEU378, LEU545 (2)	
eugenol	ILE46, PHE224, PHE356 (4), VAL359, LEU545	GLN541, TYR625
eugenol acetate	PHE224, PHE356 (3), VAL359 (2), LEU378, ILE383	GLN541, ASN544
eugenol methyl ether	ILE6, PHE224, PHE356 (3), VAL359, LEU378, LEU545	GLN541, TYR625
estragole	ALA355, VAL359, TYR425, PHE537, LEU545, TYR625, LEU626	
limonene	TYR352, ALA355, PHE356, VAL359, TYR425, LEU545	

Supplementary Table S6. Interactions between the compounds found in tarragon essential oil and OATP1B1 based on the PDB structure 8HNH. Numbers in parentheses indicate how many interactions occur for each amino acid.

8HNH	Hydrophobic interactions	H bonds	π -Stacking
Simeprevir - the ligand present in the PDB structure	THR42, PHE224, TYR352, ILE383, VAL556, ARG580	ASN213	PHE356
re-docked simeprevir	THR42, VAL349, TYR352 (2), ILE383, PHE386	ARG580	
α -pinene	PHE356 (2), THR382, PHE386 (2), LEU545		

cis- β -ocimene	TYR352, ILE353, PHE356 (5), ILE383, PHE386 (3), LEU545		
trans- β -ocimene	TYR352(2), ILE353, PHE356 (4), PHE386 (2), LEU545		
caryophyllene oxide	PRO220, PHE356 (2), ILE383, PHE386 (2)	TYR352	
eugenol	THR382, ILE383, PHE386 (2), LEU545	PHE356	
eugenol acetate	ALA216, PHE356, THR382, ILE383, PHE386	PHE386	
eugenol methyl ether	PHE356, ILE383, PHE386 (3), LEU545		
estragole	MET217, PHE356, PHE386 (2), LEU545		PHE386
limonene	THR42, PRO220, ILE383, PHE386 (5)		

Supplementary Table S7. Interactions between the compounds found in tarragon essential oil and OATP1B1 based on the PDB structure 8K6L. Numbers in parentheses indicate how many interactions occur for each amino acid.

8K6L	Hydrophobic interactions	H bonds	π -Stacking
2',7'-dichlorofluorescein - the ligand present in the PDB structure	TYR352 (4), PHE356, PHE386	GLN541, ASN544	
re-docked 2',7'-dichlorofluorescein	TYR352 (2), ALA355, PHE356	GLN541, ASN544, SER548, ARG633	TYR352
α -pinene	TYR352 (4), PHE356 (2), LEU545		
cis- β -ocimene	TYR352 (4), PHE356, PHE386	GLN541, ASN544, SER548	
trans- β -ocimene	TYR352 (3), PHE356 (2), VAL359 (2), LEU545		
caryophyllene oxide	TYR352 (3), PHE356 (3), PHE386 (2), LEU545		
eugenol	TYR352, PHE356 (2)	GLN541, ASN544, SER548	TYR352
eugenol acetate	TYR352, ALA355, PHE356, VAL359, TYR422, TYR425, LEU545, TYR625	ARG633	
eugenol methyl ether	TYR352, ALA355, LEU545		TYR352
estragole	TYR352 (3), ALA355, PHE356	GLN541	
limonene	TYR352 (3), ALA355, PHE356, TYR422		

Supplementary Table S8. Interactions between the compounds found in tarragon essential oil and OATP1B1 based on the PDB structure 9CY1. Numbers in parentheses indicate how many interactions occur for each amino acid.

9CY1	Hydrophobic interactions	H bonds	Salt bridges
α -pinene	PHE356 (2), LEU545		
cis- β -ocimene	THR42, TYR352, ILE353, PHE356 (2), PHE386, LEU545 (2)	LYS41, GLU185	LYS41
trans- β -ocimene	VAL349, TYR352, ILE353, PHE356, LEU545		
caryophyllene oxide	VAL349, TYR352, ILE353, PHE356 (2), LEU545		
eugenol	TYR352 (2), PHE356, LEU545		
eugenol acetate	TYR352 (3), LEU545		
eugenol methyl ether	TYR352 (2), LEU545		
estragole	THR382, ILE383, PHE386 (2), LEU545		PHE356

limonene	TYR352 (2), ALA355, VAL359, TYR422, LEU545		
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Supplementary Table S9. Interactions between the compounds found in tarragon essential oil and OATP1B1 based on the PDB structure 9CY3. Numbers in parentheses indicate how many interactions occur for each amino acid.

9CY3	Hydrophobic interactions	H bonds	Salt bridges	π -Stacking
atorvastatin - the ligand present in the PDB structure	THR42, TYR352, ILE353, PHE356 (2), PHE386 (2), LEU545 (2)	LYS41, GLU185	LYS41	
re-docked atorvastatin	VAL349, ILE353, PHE356 (2), LEU545, LEU579			
α -pinene	TYR352 (2), PHE356 (2), LEU545			
cis- β -ocimene	THR42, TYR352, ILE353, PHE356 (2), PHE386 (2), LEU545 (2)	LYS41, GLU185	LYS41	
trans- β -ocimene	TYR352 (2), PHE356 (2), PHE386 (3), LEU545			
caryophyllene oxide	VAL349, TYR352 (2), PHE356 (2), PHE386			
eugenol	PHE356 (2), PHE386 (2), LEU545	THR382		
eugenol acetate	TYR352, PHE356, PHE386 (4), LEU545 (2)			PHE356
eugenol methyl ether	PHE356 (2), PHE386, LEU545			PHE356
estragole	PHE356, PHE386 (2), LEU545			PHE356
limonene	PHE356 (3), ILE383, PHE386 (2), LEU545 (2)			

Supplementary Table S10. Interactions between the compounds found in tarragon essential oil and OATP1B1 based on the PDB structure 9CY4. Numbers in parentheses indicate how many interactions occur for each amino acid.

9CY4	Hydrophobic interactions	H bonds	π -Stacking
α -pinene	VAL349, TYR352 (2), PHE356, PHE386, LEU545		
cis- β -ocimene	VAL359 (2), PHE360, VAL363, THR382, PHE537, VAL538, GLN541 (2), VAL542, LEU545		
trans- β -ocimene	TYR352 (3), PHE356, PHE386 (3), LEU545		
caryophyllene oxide	VAL349 (2), TYR352 (2), ILE353, PHE386	GLY552	
eugenol	TYR352, ILE353	TYR352	
eugenol acetate	VAL349, TYR352, PHE356	GLY552	HIS555
eugenol methyl ether	TYR352, PHE356, LEU545		TYR352
estragole	TYR352, PHE356, PHE386, LEU545		PHE356
limonene	PHE356 (2), THR382, ILE383, PHE386 (3), LEU545 (2)		

Supplementary Table S11. Interactions between the compounds found in tarragon essential oil and OATP1B1 based on the PDB structure 8PHW. Numbers in parentheses indicate how many interactions occur for each amino acid.

8PHW	Hydrophobic interactions	H bonds
estrone-3-sulfate - the ligand present in the PDB structure	PHE224, PHE356 (2), LEU378, PHE386, LEU545	ASN544
re-docked estrone-3-sulfate	ALA355, PHE356 (2), VAL359, ILE383, PHE386 (2)	TYR422, ASN544
α -pinene	ILE46, PHE224 (2), PHE356 (3), LEU378, PHE386, LEU545	
cis- β -ocimene	ALA355, PHE356, VAL359, TYR362, TYR425, TYR625, LEU626	
trans- β -ocimene	TYR352, ALA355, VAL359 (2), TYR362, TYR422, TYR425, PHE537, TYR625, LEU626	
caryophyllene oxide	PHE224, PHE356 (2), VAL359, LEU378, ILE383, LEU545 (2)	
eugenol	PHE224, PHE356 (3), LEU378, LEU545	GLN541
eugenol acetate	PHE224, PHE356 (2), VAL359 (2), LEU545	
eugenol methyl ether	PHE224, PHE356 (3), VAL359	
estragole	ALA355, VAL359, TYR362, TYR422, TYR425, PHE537, TYR625	
limonene	TYR352, PHE356, VAL359, TYR425, PHE537, LEU545	

Supplementary Table S12. Interactions between the compounds found in tarragon essential oil and OATP1B3 based on the PDB structure 8PG0. Numbers in parentheses indicate how many interactions occur for each amino acid.

8PG0	Hydrophobic interactions	H bonds
α -pinene	PHE352 (2), VAL359	
cis- β -ocimene	PHE356 (5), VAL359, THR382	
trans- β -ocimene	PHE352 (2), PHE356 (2), VAL359, LEU378	
caryophyllene oxide	PHE352 (2), PHE356, THR382	
eugenol	PHE352 (2), PHE356	GLN422, GLN541, ASN544
eugenol acetate	PHE352 (2), PHE356, TYR425	GLN541, ASN544
eugenol methyl ether	PHE352, PHE356 (3)	ASN544, SER548
estragole	PHE352 (3), PHE356 (2)	GLN422, ASN544
limonene	PHE352 (2), PHE356, VAL359, LEU378	