PREDICTING MOLECULAR PROPERTIES AND BIOACTIVITY SCORE OF SIMILAR COMPOUNDS OF TAZAROTENE

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Abstract

The purpose of present work was to define with a Tanimoto similarity metric of 0.8 similar compounds of tazarotene and to predict and analyze theirs molecular physicochemical properties and bioactivity score by the CompTox Chemistry Dashboard and Molinspiration software. The data analysis for the three similar compounds of tazarotene were found to have close molecular properties and structural features and their bioactivity score is active.

Material and Methods

Tazarotene is a third-generation retinoid with CAS number 118292-40-3 (Figure 1).

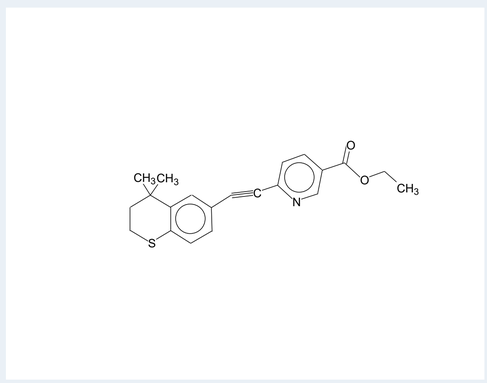


Figure 1. Structure of tazarotene

CompTox Chemistry Dashboard. The Dashboard is a freely accessible web-based application and data hub providing access to data associated with chemical substances. It accesses data from nine component databases housing generic data types. The Dashboard also integrates data from other platforms (specifically PubChem and PubMed) via web services and visualization widgets. The Dashboard represents a first step in building a comprehensive chemical substance- centric informatics architecture to provide flexible access to data, models and analysis tools in support of EPA's research programs (USA EPA, CompTox Chemistry Dashboard).

Similar molecules. The similar molecules tab shows the results of a structural similarity search, underpinned by a Tanimoto similarity calculated using the Bingo Molecular Search Cartridge (with the associated Indigo fingerprints) ("Epam" Bingo PostGreSQL cartridge). The search displays up to 50 of the top-most similar molecules above a Tanimoto similarity metric of 0.8. The view also displays a selection of experimental and predicted chemical properties to help illustrate the consistency and concordance of these attributes within the identified set of structurally related molecules (USA EPA, CompTox Chemistry Dashboard).

Molinspiration software. The Molinspiration software was used for calculation of important molecular properties (logP, polar surface area, number of hydrogen bond donors and acceptors and others), as well as prediction of bioactivity score for the most important drug targets (GPCR ligands, kinase inhibitors, ion channel modulators, nuclear receptors) (Molinspiration Chemoinformatic Software).

Results

Three similar tazarotene structures with a Tanimoto similarity metric of 0.8 (from 0.92 to 0.84) by the CompTox Chemistry Dashboard were found. The similar tazarotene compounds are presented in Table 1.

Table 1. Results of similar tazarotene structures

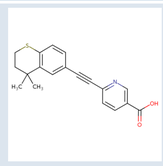
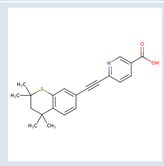
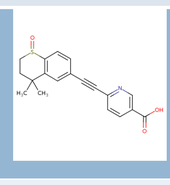
№	CAS number	Name of compound	Structure of compound	Simi larity
11	118292-41-4	6-((3,4-dihydro-4,4-dimethyl-2H-1-benzothiopyran-6-yl)ethynyl)- 3-pyridinecarboxylic acid		0.92
22	145352-11-0	6-[(2,2,4,4-Tetramethyl-3,4-dihydro-2H-1-benzothiopyran-7-yl)ethynyl]pyridine-3-carboxylic acid		0.88
33	603952-64-3	6-[(4,4-Dimethyl-1-oxo-1,2,3,4-tetrahydro-1-benzothiopyran-6-yl)ethynyl]pyridine-3-carboxylic acid		0.84

Table 2. Calculated data for molecular physicochemical properties of similar compounds of tazarotene.

Name of compound	A_1	A_2	A_3	A_4	A_5	A_6	A_7	A_8	A_9
6-((3,4-dihydro-4,4-dimethyl-2H-1-benzothiopyran-6-yl)ethynyl)- 3-pyridinecarboxylic acid	3.42	50.19	23	323.42	3	1	0	1	290.96
6-[(2,2,4,4-Tetramethyl-3,4-dihydro-2H-1-benzothiopyran-7-yl)ethynyl]pyridine-3-carboxylic acid	4.23	50.19	25	351.47	3	1	0	1	323.78
6-[(4,4-Dimethyl-1-oxo-1,2,3,4-tetrahydro-1-benzothiopyran-6-yl)ethynyl]pyridine-3-carboxylic acid	1.82	67.26	24	339.42	4	1	0	1	298.50

*The following properties are available:
A_1: LogP - octanol-water partition coefficient; A_2: TPSA - polar surface area; A_3: natoms - number of nonhydrogen atoms; A_4: MW - molecular weight; A_5: nON - number of hydrogen-bond acceptors (O and N atoms); A_6: Nohnh - number of hydrogen-bond donors (OH and NH groups); A_7: nviolations - number of Rule of 5 violations; A_8: nrotb - number of rotatable bonds; A_9: volume – molecular volume.

Table 3. Calculated data for bioactivity score of the three compounds of tazarotene

Name of compound	A_1	A_2	A_3	A_4	A_5	A_6
6-((3,4-dihydro-4,4-dimethyl-2H-1-benzothiopyran-6-yl)ethynyl)-3-pyridinecarboxylic acid	0.41	0.01	0.16	0.84	0.22	0.60
6-[(2,2,4,4-Tetramethyl-3,4-dihydro-2H-1-benzothiopyran-7-yl)ethynyl]pyridine-3-carboxylic acid	0.41	-0.03	0.13	0.98	0.29	0.71
6-[(4,4-Dimethyl-1-oxo-1,2,3,4-tetrahydro-1-benzothiopyran-6-yl)ethynyl]pyridine-3-carboxylic acid	0.64	0.16	0.47	0.77	0.29	0.78

*The following properties are available:
A_1: GPCR ligand; A_2: Ion channel modular; A_3: Kinase inhibitor; A_4: Nuclear receptor ligand; A_5: Protease inhibitor; A_6: Enzyme inhibitor.

Acknowledgements

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References

1. USA EPA, CompTox Chemistry Dashboard, URL: https://comptox.epa.gov/dashboard/
2. Molinspiration Chemoinformatic Software, URL: https://www.molinspiration.com/