| About section of a profiler |
|---|
| **Name of the profiler** |
| Estrogen receptor binding |
| **Developer; date; version** |
| ***Developer:***<br>Laboratory of Mathematical Chemistry (LMC), Bourgas, Bulgaria<br><br>***Donator:***<br>Laboratory of Mathematical Chemistry (LMC), Bourgas, Bulgaria and Schultz, T.W, Ph.D. The University of Tennessee, College of Veterinary Medicine, Knoxville TN USA<br><br>***Version*:** 2.2<br>December 2016 |
| **Relevance/Applicability to endpoint(s)** |
| Estrogen receptor (ER) binding is a molecular initiating event much like protein binding. It is an endpoint where several comprehensive databases exist, which has led to the development of several approaches for using (Q)SARs to predict ER binding and possible subsequent endocrine disruption. Since the RE-binding is a receptor mediated event, particular organic functional groups, size and shape are critical to binding potency. Based on the latter profiler consist of seven categories associated with positive ER binding effect and four categories associated with negative ER binding effects. Both list of categories are provided below:<br>• ***Very strong binders, OH group***<br>• ***Strong binder, NH2 group***<br>• ***Strong binder, OH group***<br>• ***Moderate binder, NH2 group***<br>• ***Moderate binder, OH group***<br>• ***Weak binder, NH2 group***<br>• ***Weak binder, OH group***<br>Chemicals with a single 5-or 6-member carbon ring structure with an unhindered amino-group (-NH2) or hydrohyl group (one in the para- or meta-position on the ring) (5) are ER binders with different potency range.<br>• ***Non-binder, with impaired OH or NH2 group***<br>• ***Non-binder without OH or NH2 group***<br>• ***Non-binder, non-cyclic structure***<br>• ***Non-binder, MW > 500***<br>Chemicals that have a molecular weight of less than 500, but do not possess a cyclic structure are reported to non-binders to the receptor. Also chemicals that have a molecular weight less than 500, and possess a cyclic structure but without a hydroxyl or amino group are reported to be non-binders to the receptor. In this group are included chemicals with cycles and MW =<500 and all their OH and NH2 groups attached to 5 or 6 C-atoms ring are impaired and chemicals with MW > than 500 Da. |
| **Relevance/Applicability to particular chemical classes** |
| This profiler is applicable to organic chemicals that have aromatic ring, bounded with hydroxylic group, or amino group and their derivatives. |
| **Approach used to develop the profiler -** Concise but informative description of: |
| a) The aim of the profiler was to identify chemicals associated with organic, low molecular weight chemicals associated with estrogenic binding potency of chemicals. |

b) The profiler include list of seven categories associated with estrogenic binding potency and four category associated with non-binding potential. Each of the categories is codded by the specific structural boundary along with the logKow or molecular weight parametric boundary.

c) Summary list of the profiles/categories is provided below

**Summary list of profiles/alerts within the profiler**

| Profile/structural alert | Phys-chem parameter |
|---|---|
| ***Very strong binders, OH group*** | MW between 200 -500 Da |
| ***Strong binder, NH2 group*** | MW between 200 -500 Da |
| ***Strong binder, OH group*** | MW between 200 -500 Da |
| ***Moderate binder, NH2 group*** | MW between 170 -200 Da |
| ***Moderate binder, OH group*** | MW between 170 -200 Da |
| ***Weak binder, NH2 group*** | MW < 170 Da |
| ***Weak binder, OH group*** | MW < 170 Da |
| ***Non-binder, with impaired OH or NH2 group*** | MW < 500 Da |
| ***Non-binder without OH or NH2 group*** | MW < 500 Da |
| ***Non-binder, non-cyclic structure*** | MW < 500 Da |
| ***Non-binder, MW > 500*** | MW >500 Da |

**Similar to other profilers**

No similarity with other Toolbox profilers

**Short description of update version**

SMARTS language for describing molecular patterns, i.e. structural boundaries, structural alerts has been implemented in OECD QSAR Toolbox 4.0. As a result ***Estrogen Receptor Binding*** has been rewritten but without modifying the knowledge and/or the logic they are based on. Only small distinctions are expected in the profiling results between Toolbox v.3.4 and v 4.0 due to different interpretation of the molecular structures, e.g. for heterocyclic/heteroaromatic compounds.

**Disclaimer**

The structural boundaries used to define the chemical classes (e.g. “Alcohol” – chemical class from “Organic functional group” profiler) or alerting groups responsible for the binding with biological macromolecules (e.g. “Aldehydes” – structural alert for protein binding), represent structural functionalities in the molecule which could be used for building chemical categories for subsequent data gap filling. They are not recommended to be used directly for prediction purposes (as SARs).