



青蒿素类药物性数据分析

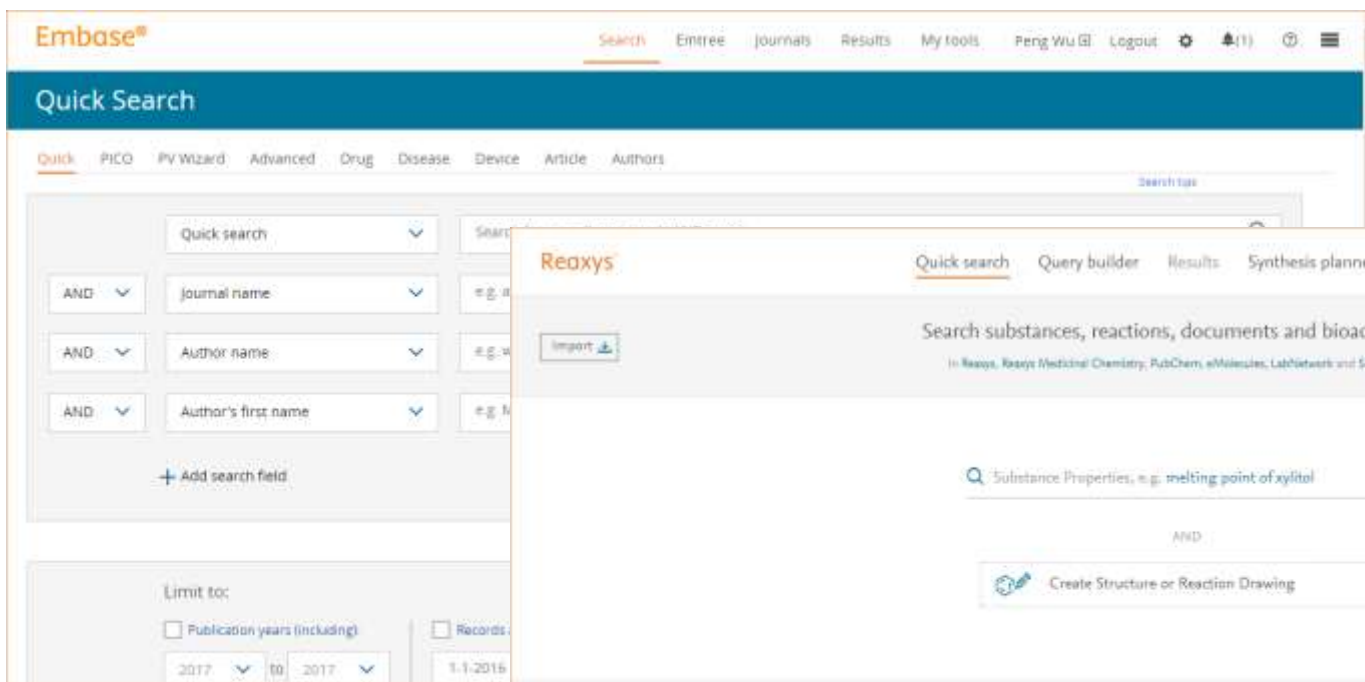
Presented By

Date

通过RMC模块+Embase数据库分析青蒿素类药性

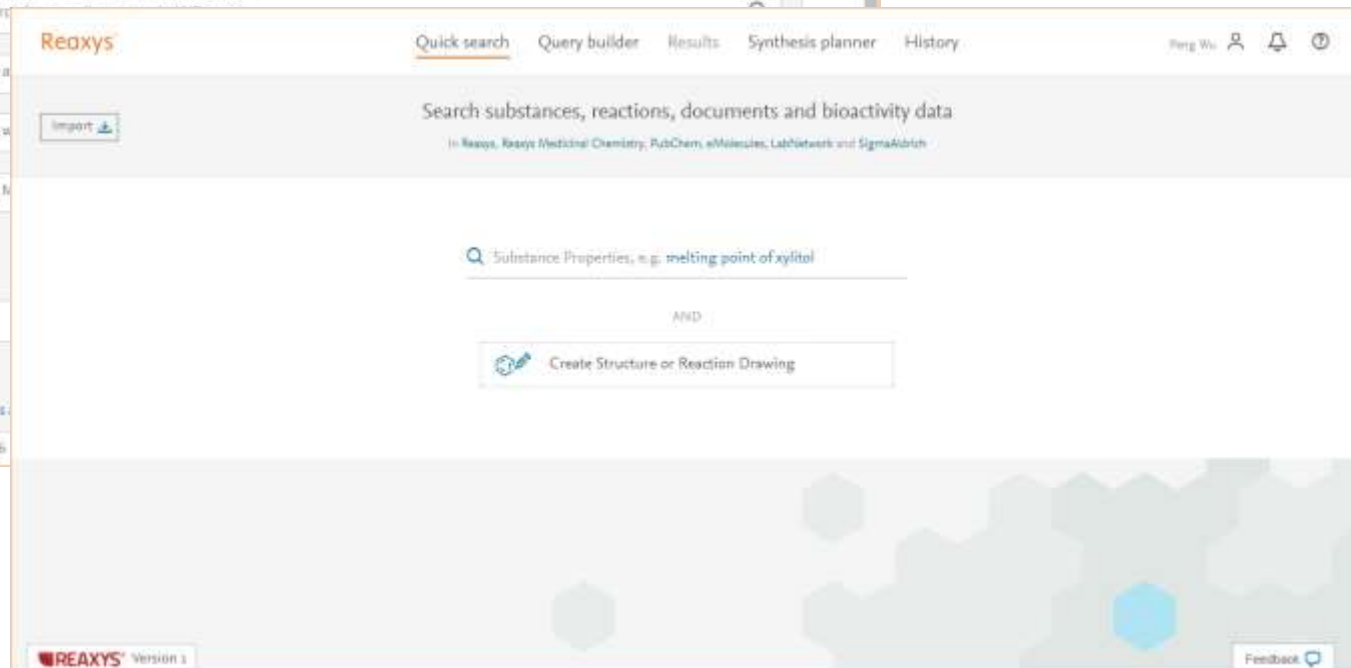
案例分析：

1. 检索‘青蒿素’相关报道
2. 检索‘青蒿素及其报道过的衍生物’结构各项生物活性数据
3. 分析已报道过的‘青蒿素结构改变’对‘青蒿素及其衍生药物’的成药性贡献



The screenshot shows the Embase database interface. At the top, there is a navigation bar with 'Search', 'Emtree', 'Journals', 'Results', 'My tools', 'Peng Wu', and 'Logout'. Below this is a 'Quick Search' section with tabs for 'Quick', 'PICO', 'PV Wizard', 'Advanced', 'Drug', 'Disease', 'Device', 'Article', and 'Authors'. The 'Quick' tab is selected. There are three search fields with 'AND' operators: 'Journal name', 'Author name', and 'Author's first name'. Below these is an 'Add search field' button. At the bottom, there is a 'Limit to:' section with checkboxes for 'Publication years (including)' and 'Records', and a date range selector set to '2017 to 2017'.

Embase数据库跟踪相关药物的各方面最新报道，包括安全性监控等信息



The screenshot shows the Reaxys database interface. At the top, there is a navigation bar with 'Quick search', 'Query builder', 'Results', 'Synthesis planner', and 'History'. Below this is a search bar with the text 'Search substances, reactions, documents and bioactivity data'. There is an 'Import' button and a search field with the text 'Substance Properties, e.g. melting point of xylitol'. Below the search field is an 'AND' operator and a 'Create Structure or Reaction Drawing' button. At the bottom, there is a 'REAXYS Version 1' logo and a 'Feedback' button.

RMC模块提供，基于报道的实验数据的直接分析结果

检索内容系统化

The screenshot displays the Reaxys Structure editor. At the top, there are navigation tabs: Quick search, Query builder, Results, Synthesis planner, and History. The user's name, Peng Wu, is visible in the top right corner. The main workspace shows a chemical structure of a complex molecule with multiple rings and stereocenters. A yellow callout box labeled '名字导入结构' (Import structure by name) points to the 'Create structure template from name' button. To the right, a search options panel is visible, with 'As substructure' selected and 'Stereo' unchecked. Two orange arrows point from the Chinese text annotations to the 'On all atoms' radio button and the 'Stereo' checkbox in the search options panel.

名字导入结构

Create structure template from name >

亚结构检索，确保碳骨架不变

光学异构保护关闭

Search this structure as:

- As drawn
- As substructure
 - On all atoms
 - On heteroatoms
- Similar
- Tautomers
- Stereo
- Additional ring closures
- Related Markush
- Salts
- Mixtures
- Isotopes
- Charges
- Radicals

+ More options

Clear

首先，通过结构，把‘青蒿素’相关的衍生物，盐型都检索出来。

检索要点：以‘青蒿素’为母核，‘亚结构检索’，‘关闭光学异构保护’开启‘互变异构’+‘Markush结构’等按钮

数据归纳

The screenshot displays the Reaxys search results page. The top navigation bar includes 'Quick search', 'Query builder', 'Results' (selected), 'Synthesis planner', and 'History'. The user 'Peng Wu' is logged in. The main header shows '593 Substances out of 2,695 Documents, containing 1,622 Reactions, 90 Targets'. A sidebar on the left lists various filters, with 'Parameters' highlighted. The main content area shows a list of substances, with the first entry, 'Reaxys ID: 4194670', having its 'Druglikeness' filter highlighted in orange. The second entry is 'artemisinin' with 'Druglikeness' also highlighted. The third entry is also 'artemisinin'. The interface includes a 'Feedback' button in the bottom right corner.

Substance	Reaxys ID	Chemical Formula	Druglikeness	Bioactivity (All)	Spectra	Other Data	Preparations	Reactions	Targets	Documents
1	4194670	C ₁₅ H ₂₂ O ₅	282.337	4194670	63968-64-9	102	108	902	65	2,371
2	artemisinin	C ₁₅ H ₂₂ O ₅	282.337	22468165	3	1	6	13	108	
3	artemisinin	C ₁₅ H ₂₂ O ₅	282.337	5754123	63968-64-9, 113472-97-2, 119241-68-8	31				

从‘druglikeness’中可以看到并且导出LogP数据，通过整理以后，能够协助的‘SPR’性效关系的分析。

类药性数据收集-LogP

The screenshot displays a chemical database interface with the following elements:

- Header:** 593 Substances out of 2,695 Documents, containing 1,622 Reactions, 90 Targets
- Navigation:** 0 selected, Limit To, Exclude, Export (highlighted)
- Substance Details:**
 - Reaxys ID: 4194
 - Chemical formula: $C_{15}H_{22}O_3$, 282.337
 - Identification
 - Druglikeness
- Chemical Structure:** A complex polycyclic molecule with multiple hydroxyl groups and a lactone ring.
- Identification Panel:**
 - Identification
 - Druglikeness
- Lipinski rules component table:**

Lipinski rules component	
Molecular Weight	282.337
logP	3.039
HBA	5
HBD	0
- Export substances Reaxys dialog:**
 - Choose a format: PDF/Print
 - Range: All results - 593
 - Export options:
 - All available data
 - Identification data only
 - Hit data only
 - Choose specific data + Add datapoints
 - Additional options:
 - Include structures
 - Include a description in the o...
- Export substances dialog:**
 - Medical Chemistry (checked)
 - Other Data: 12
 - Physical Data: 142
 - Spectra: 185
 - Bioactivity: 448
 - Druglikeness: 448

既可以直观查看，也可以，根据需要的格式导出

具体生物活性数据的查看

完整版的Reaxys已经把文献和专利中的生物活性数据‘具体数值’进行了摘录

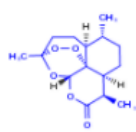
Filters and Analysis

- By Structure ▾
- Measurement pX ▾
- Highest Clinical Phases ▾
- Targets ▾
- Parameters ▾
- Substance Classes ▾
- Molecular Weight ▾
- Availability ▾
- Availa
- Availa

593 Substances out of 2,695 Documents, containing 1,622 Reactions, 90 Targets

0 selected Limit To Exclude Export

1




Reaxys ID: 4194670
 $C_{15}H_{22}O_5$ 282.337 4194670 63968-64-9

Identification Bioactivity (All) Spectra - 102 Preparations - 108 >
 Druglikeness Physical Data - 375 Other Data - 213 Reactions - 902 >
 Targets - 65 >
 Documents - 2,371 >

Heatmap

Sort by No of References ▾

2



artemisinin
 $C_{15}H_{22}O_5$ 282.337 22468165

Identification

Reaxys - 593 ▾

Bioactivity (All)

- ▾ In vitro: Efficacy - 1,358
- ▾ In vivo: Animal Model - 135
- ▾ Metabolism - 160
- ▾ Pharmacokinetic - 98
- ▾ Toxicity/Safety Pharmacology - 343

In vivo: Animal Model - 135

Quantitative Results

pK	Parameter	Value (qual)	Value (quant)	Unit	Biological Species	Animal Model	Route of administration	Dose	Dosing regimen	Effect
6.33	IC50		7.1	nM	human					Antifungal
7.42	% Inhibition		25	%	chicken		topical administration	5 nM	Single	
8.87	% Increase	Active			Sprague-Dawley rat	experimental retinal degeneration		30 - 300 µg/ml		Photoprotective
8.97	% Increase	Active			Sprague-Dawley rat	experimental retinal degeneration		30 - 300 µg/ml		Photoprotective

‘SAR’ 构效关系的构建-Target to substance

通过构建不同的 ‘SAR’ 可以快速的分析，预估结构修饰以后药效可能的结果

首先，Heatmap可以快速概览，‘青蒿素及其衍生物’，测试过的靶点与化合物的构效关系

593 Substances out of 2,695 Documents, containing 1,622 Reactions, 90 Targets

0 selected Limit To Exclude Export

Reaxys ID: 4194670
C₁₅H₂₂O₅ 282.337 4194670 63968-64-9

Identification Bioactivity (All) Spectra - 102 Preparations - 108 >
Druglikeness Physical Data - 375 Other Data - 213 Reactions - 902 >
Targets - 65 >
Documents - 2,371 >

Heatmap settings

Value of X-axis: **Targets**

Value of Y-axis: **Substances**

Value of Cells: **Maximum of pX**

Show substances: Names Structure drawing

Display mode: Normal Full Screen

Always show settings Apply >

根据参数的不同可以构建不同的SAR构效关系，SPR性效关系，为分子结构的药理学改进，提供辅助和参考。

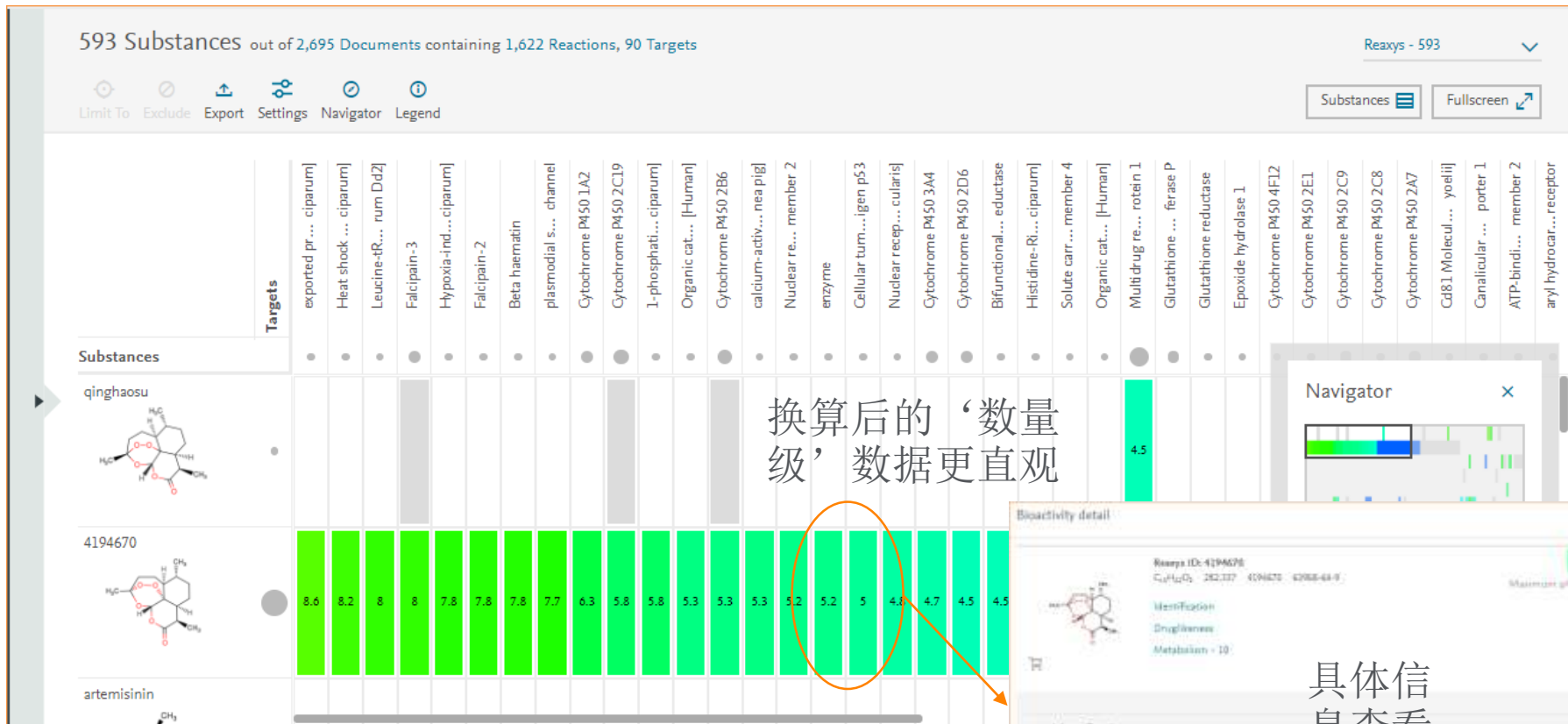
Targets

- Bioassays
- Targets
- Target Species
- Biological Species
- Effects
- Parameter
- Cell Lines
- Substances

参数设置菜单打开后，可选参数

靶点-化合物, 构效关系总览

横坐标为, 相关化合物测试过的靶点, ‘包含适应症靶点’ + ‘脱靶靶点’



纵坐标, 青蒿素及其衍生物。该SAR构效关系可以导出Excel的表格, 便于整理和分析

衍生物改构对单一生物活性数据贡献度分析-IC50

Reaxys数据库通过各种‘Filter’进行‘单一生物活性数据’的‘改构分析’，把已经报道过的各种‘基于母核的衍生物’通过改构以后，对‘特定生物活性贡献度’进行分析，从而参考和辅助药物分子‘改构设计’。

The image displays two screenshots of the Reaxys 'Filters and Analysis' interface. The left screenshot shows the 'Parameters' menu highlighted in yellow, with an orange arrow pointing to the right screenshot. The right screenshot shows the 'Parameters' menu expanded, with 'ic50' selected and highlighted in yellow. The 'ic50' parameter has a red progress bar and the value '227'. Other parameters listed include 'qualitative' (186), 'ec50' (87), 'activity' (72), 'therapeutic index' (36), '% inhibition' (20), and 'number' (12). The main content area shows a list of substances, including 'artemisinin' with its chemical structure and Reaxys ID: 4194670.

Parameter	Count
ic50	227
qualitative	186
ec50	87
activity	72
therapeutic index	36
% inhibition	20
number	12

打开
‘Parameters’
菜单，
选择限制为
‘IC50’
数据

筛选后构建IC50-化合物， SAR构效关系图

Heatmap settings ×

Value of X-axis: **Substances** ✓

Value of Y-axis: **Parameter** ✓

Value of Cells: **Maximum of pX** ✓

Show substances: Names Structure drawing

Display mode: Normal Full Screen

Always show settings Apply >

限定好IC50参数以后，构建SAR构效关系图时，设置X,Y轴分别为，化合物和特定参数即可。

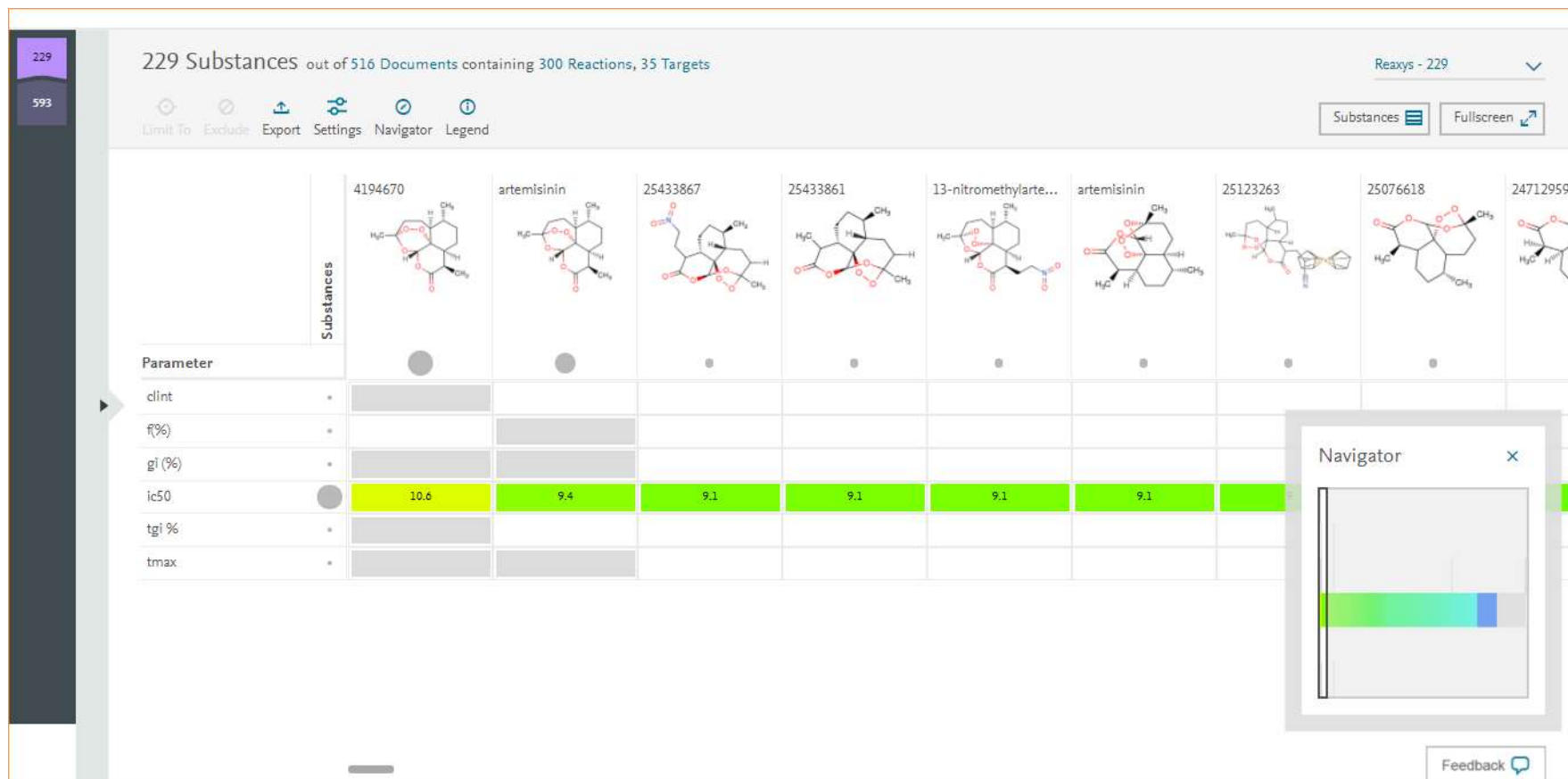
如果需求，‘单一参数’的SAR构效关系，如：clint-substance；F%-substance等，请按相同方式构建



快速获得227个‘青蒿素’及其不同衍生物+盐型的IC50数据总览，假如‘青蒿素’在‘溶解性’；‘清除率’；‘生物利用度’不够好的话，那我们从已经报道过的各种衍生物着手，优先筛选出IC50较高的衍生物，异构体，盐型，参考这些结构，确立最初的改构方向。

当然，也可以，建立不同‘单一生物活性’的SAR构效关系，综合参考结构设计。

综合型SAR构效关系快速组建 (clint; AUC; F%.....)



同过‘综合构效关系’能够快速检索到，综合药性较好的结构，可以参考其设计的新结构的同时，也给出了提示，是否‘新设计的分子’与‘报道过分子’存在侧链重合或相似时，是否要把‘新设计的分子’可能不好的数据优先进行测试。