MARKUSH FOR PATENT SEARCH AND ANALYSIS

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ChemAxon UGM San Diego 2013

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THOMSON REUTERS MARKUSH DATA

- Indexing for 2.6 million patent families
  - 1.6m Markush structures, re-drawn & stored in Thomson Reuters vmn file format
  - 2.15m specific compounds
  - plus the corresponding DWPI records
  - 28 patent issuing authorities covered
    - backfile from 1978 for US, EP and WO patents
  - covers pharmaceutical, agrochemical and general chemistry patents
- Indexed as part of the editorial process that creates Derwent World Patents Index (DWPI)
  - Informative English language titles & abstracts from worldwide patents
  - Patent family listing, patent assignees

COVERAGE START DATES

Austria	1987	**Korea**	2008
Australia	1987	**Malaysia**	2010
Belgium	1987	**Netherlands**	1987
Brazil	2010	**New Zealand**	1987
Canada	1987	**PCT/WO**	1978 (Pharma); 1982 (Agro + Gen. Chem.)
China	2008	**Poland**	2011
European Patents	1978 (Pharma); 1982 (Agro + Gen. Chem.)	**Russia**	1993-1998 and 2010 to date
France	1961-1976 (FR-M); 1978 (Pharma); 1982 (Agro + Gen Chem)	**South Africa**	1987
Germany	1980 (Pharma); 1983-84 and 1987 to date (Agro + Gen. Chem.)	**Spain**	2010
Great Britain	1980 (Pharma); 1983-84 and 1987 to date (Agro + Gen. Chem.)	**Sweden**	1987
Gulf Cooperation Council	2008	**Switzerland**	1987
India	2000	**Thailand**	2010
Ireland	1987	**United States**	1978 (Pharma); 1982 (Agro + Gen. Chem.)
Japan	1987	**Vietnam**	2010

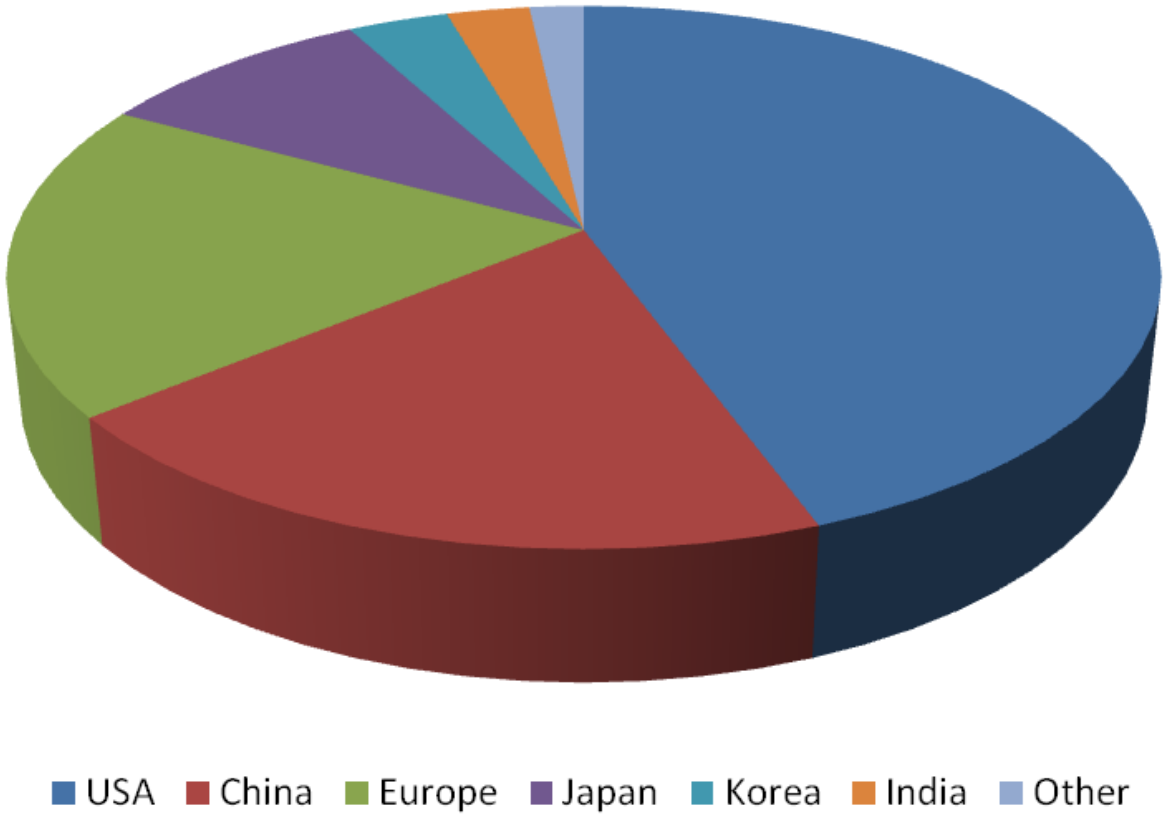
MARKUSH PATENT ANALYSIS

- What can analysis of Markush and DWPI patent data tell us about global patenting trends in 2012?
- > 8000 patents claiming new pharmaceutical Markush structures
- > 3700 patents claiming new non-pharma Markush structures

MARKUSH PHARMA PATENTING COMPANIES 2012

Number of patents	Company
129	MERCK & CO
119	ROCHE
82	BAYER AG
60	ABBOTT
59	GLAXOSMITHKLINE
57	NOVARTIS
57	CENTRE NATIONAL RECHERCHE SCIENTIFIQUE
55	BOEHRINGER INGELHEIM
54	SANOFI AVENTIS
52	BRISTOL-MYERS SQUIBB
51	MERCK PATENT GMBH
42	JOHNSON & JOHNSON
41	ALLERGAN
39	TAKEDA PHARMA
37	PFIZER
30	COUNCIL SCI&IND RES INDIA
27	SHIONOGI
26	DAIICHI SANKYO
25	UNIV CALIFORNIA

MARKUSH PHARMA PATENTING TERRITORIES IN 2012



MARKUSH DATA ACCESS

- Markush structure data available alongside corresponding specific compounds & DWPI records
- Loads into ChemAxon's JChem database tools
  - In-house or new cloud-hosted solution
- Resulting solution gives access to full chemistry & patents dataset
  - data can be searched, enumerated & integrated into the customer's own systems & workflows

MARKUSH ON CHEMAXON 2013

Markush 2013	Benefits
New cloud-hosted product, previously only in-house solution available	Saves the customer setting up their own IT infrastructure to host the data & platform
Large increase in search speed, now comparable or faster than Questel	Results appear more quickly, reduced time spent on searching
Revised user-interface	Easier to use, more DWPI fields now included
New export options	User can create reports with structures and DWPI abstracts together
Improved search algorithms	More reliable structure search results
Benchmarked against Questel	Assures reliability and demonstrates unique results compared to Questel
Customer working group active since mid-2012 to advise on product needs	Tailors ongoing developments to user needs
Additional 1978-1987 data backfile added	Parity to Questel and CAS
Further features to be added in 2014	Continuous product improvement

CHEMAXON – MARKUSH WORKING GROUP FEEDBACK

- ***General feedback summary: the product provides direct access to Markush structure data, offering high volume search capability coupled with unique visualization and structure mining features***
- Working Group comments:
  - "*This system is much more than just replacing MMS data, e.g. data visualization, white space analysis. Don't see this functionality coming from anywhere else."*
  - *"Once the quality is known (benchmarking with MMS), then there is no point in waiting to start the service"; "Provides graphical views of Markush structures that are not possible with other tools"*
  - *"We liked having access to the Markush structures for an invention"; "The invention details are well laid out"*

MARKUSH BENCHMARKING

Objective: To demonstrate the utility of ChemAxon system, the Markush Working Group requested benchmark searches for 50 drug molecules comparing results for ChemAxon against MMS on Questel

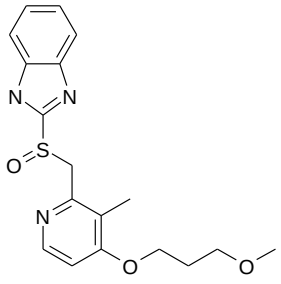
Results: 84% overlap to MMS achieved for the full structures and 78% for the generic searches, a good result as there is inherent 'fuzziness' in Markush structure searching

In addition the ChemAxon search retrieved relevant results not found by Questel, e.g. a search for the antiulcer drug rabeprazole, ChemAxon found 12 patents not retrieved by the Questel MMS search engine

RABEPRAZOLE – UNIQUE HITS FROM CHEMAXON

Patent	Assignee	DWPI Title
WO2008017020	DR REDDY'S	Preparing benzimidazole-type compound, useful as proton pump inhibitors, comprises reacting benzimidazole compound with oxidizing agent
WO2007138468	WOCKHARDT LTD	Preparation of benzimidazole sulfinyl compounds, useful to treat ulcer diseases, comprises oxidizing thioether compound in presence of oxygen scavenger with oxidizing agent in organic solvent
WO2007017244	SANDOZ AG	Preparation of 2-(2-pyridylmethyl)sulfinyl-1H-benzimidazole compound useful for making pharmaceutical composition involves crystallizing slurry of the compound from solvent or mixture of solvents comprising a quaternary amine compound
WO2003008406	JANSSEN PHARM NV	Preparation of benzimidazole-sulfoxide derivatives useful in treatment ofgastro-esophageal reflux, gastritis, duodenitis, gastric and duodenal ulcers, comprising oxidation of sulfide and selective removal of sulfone by-product
WO2001079194	ESTEVE QUIMICA SA	2-(Pyridylthiomethyl)-benzimidazole derivative preparation for use as intermediate for antiulcer agents, by reacting 2-methyl-pyridine-N-oxide with carboxylic or sulfonic anhydride then 2-mercapto-benzimidazole
JP2001270827	EISAI CO LTD	Physicochemically stabilized tablets comprising benzimidazole compounds or their salts, useful as antiulcer medicaments
WO2001028559	EISAI CO LTD	Stabilizing a benzimidazole compound using crospovidone for use in peroral compositions
JP2000355540	EISAI CO LTD	Composition used for treating gastric and duodenal ulcers contains benzimidazole compound and e.g. sodium hydroxide
WO2001004109	QUIMICA SINTETICA SA	Preparation of 2-(2-pyridinylmethylsulfinyl)-1H-benzimidazole derivatives used for treating ulcers by substituting corresponding 4-halo- or 4-nitro-substituent in pyridine ring with alkoxide
WO1999002521	EISAI CO LTD	Preparation of benzimidazole sulphoxide compounds - by oxidising thioether compound using e.g. perborate salt and acid anhydride catalyst
WO1997025064	ASTRAZENECA AB	Oral dosage form comprising a proton pump inhibitor and a non-steroidal anti-inflammatory drug - prevents gastrointestinal side-effects associated with non-steroidal anti-inflammatory drug treatment and has proton pump inhibitor protected by an enteric coating layer
WO1996002535	ASTRAZENECA AB	Enantiomeric synthesis of sulphoxide cpds., e.g. omeprazole - comprises oxidising pro-chiral sulphide using an oxidising agent, a chiral titanium complex and opt. a base

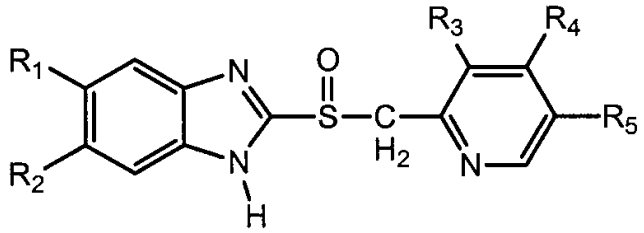
RABEPRAZOLE – UNIQUE HITS FROM CHEMAXON [1]



Rabeprazole

Claims:

1. A process for preparing proton pump inhibitors of the benzimidazole-type having Formula (I) and their salts

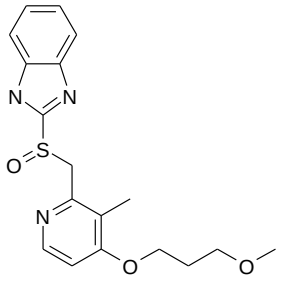


Formula (I)

Structure matches rabeprazole when
R_1, R_2, R_5 = H;
R_3 = Me
R_4 = Methoxypropoxy

wherein R_1 and R_2 are the same as or different from each other and are selected from hydrogen, methoxy or difluoromethoxy, R_3, R_4 and R_5 are the same as or different from each other and are selected from hydrogen, methyl, methoxy, methoxypropoxy or trifluoroethoxy, which process comprises:

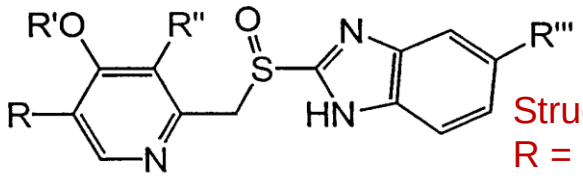
RABEPRAZOLE – UNIQUE HITS FROM CHEMAXON [2]



Rabeprazole

WO2001004109 **CLAIMS**

1.- Procedure for obtaining derivatives of 2-(2-pyridinilmethylsulphinyl) - 1*H*-benzimidazole of general formula (I):



(I)

Structure matches when
R = H
R' = methoxypropyl
R'' = methyl
R''' = H

including their corresponding metal or quaternary ammonium salts, such as the salts of Li, Na, K, Mg, Ca, Ti, NR_4 (where R is a C_{1-4}-alkyl radical), in which:

R represents an atom of hydrogen or an alkyl radical such as methyl

R' represents an alkyl chain, which may or may not be interrupted by an atom of oxygen, such as methyl and 3-methoxypropyl;

R'' represents an alkyl or alkoxy radical such as methyl and methoxy;

R''' represents an atom of hydrogen or an alkoxy remnant

SOLUTION ORIENTED BENEFITS

- Convenience and time-saving of having Markush structures, specific compounds and English language DWPI summaries integrated together in a single platform
- Query structures are displayed in context within the hit Markush structures, saving the user time in identifying key hits from a results set
- ChemAxon’s enumeration features unlock a Markush structure to allow the user to see the real compounds described within.
- Enumerated structures can be exported in standard chemical data formats, allowing potential integration into other analysis tools

USE CASES

- Novelty & freedom to operate searching by IP departments
  - Easy assessment of structural proximity of query structure to hit Markush
- Screening of new structures against existing IP
- Potential use in white-space identification, patent busting etc.
- Creation of libraries of specifics for use in other systems

DEMO OF CHEMAXON'S SEARCH & ENUMERATION OF MARKUSH

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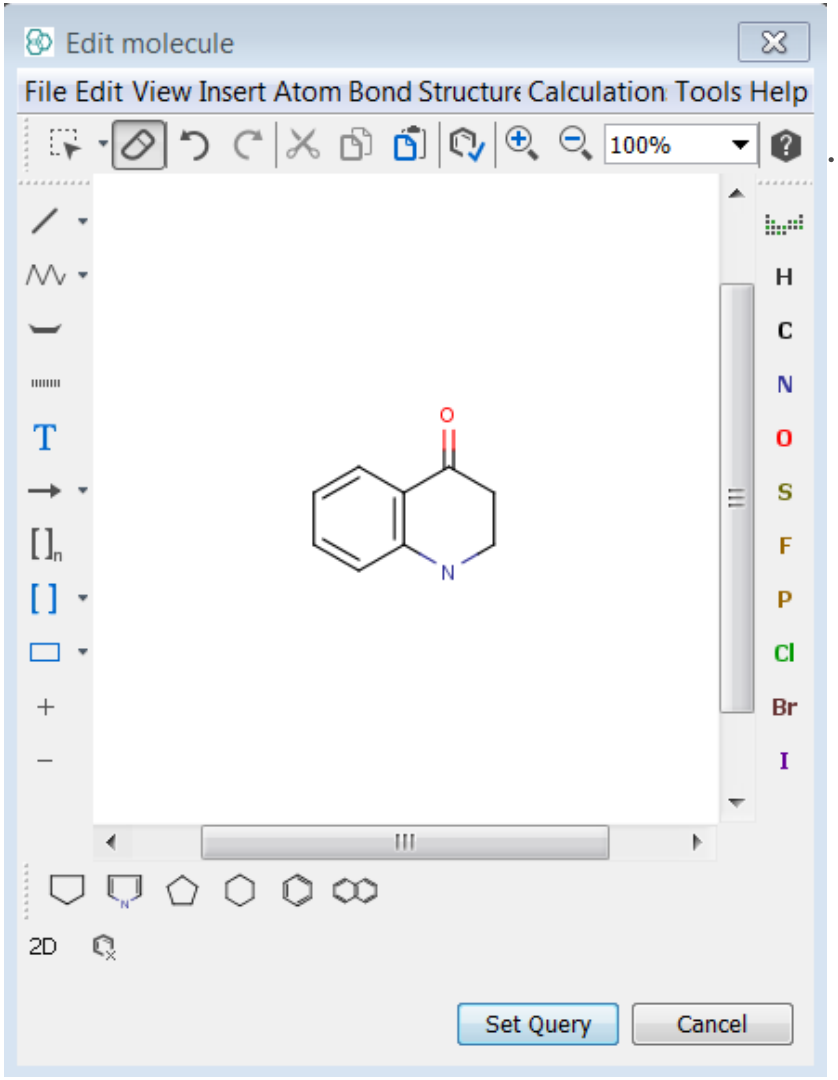

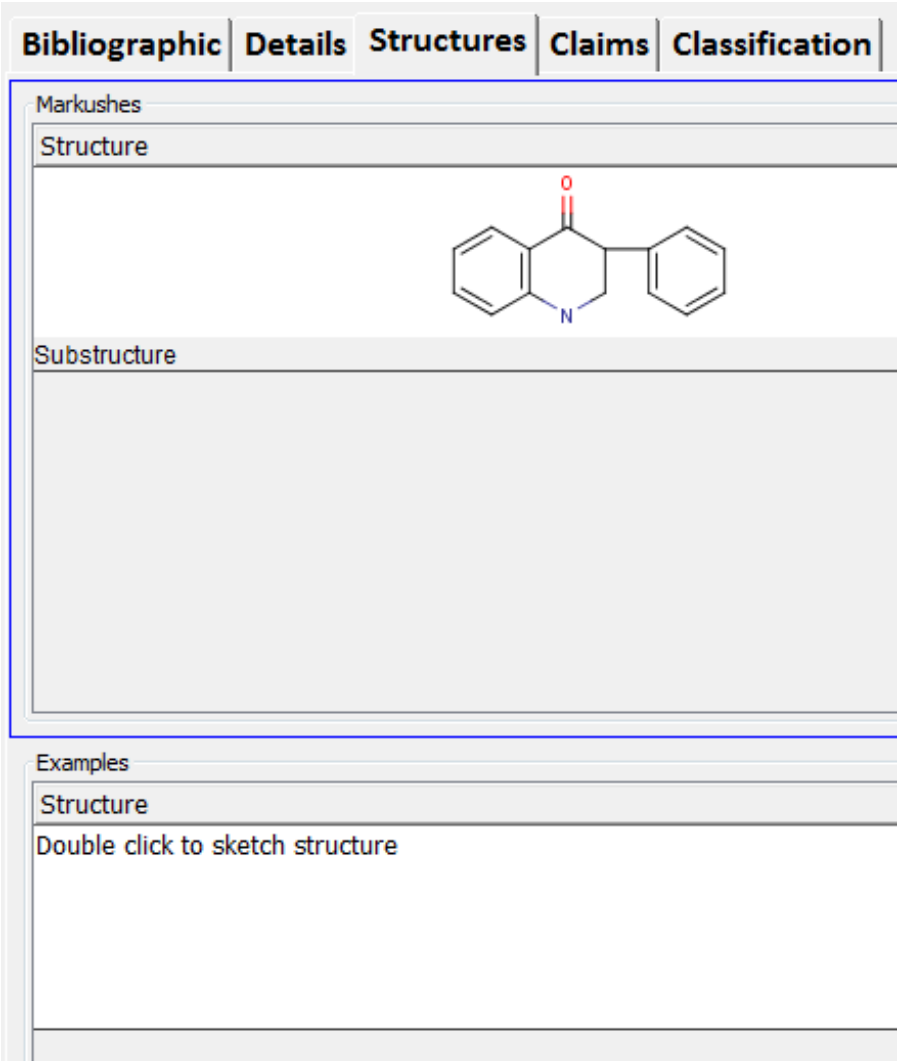

Draw the structure

Substructure search against the Markush dataset

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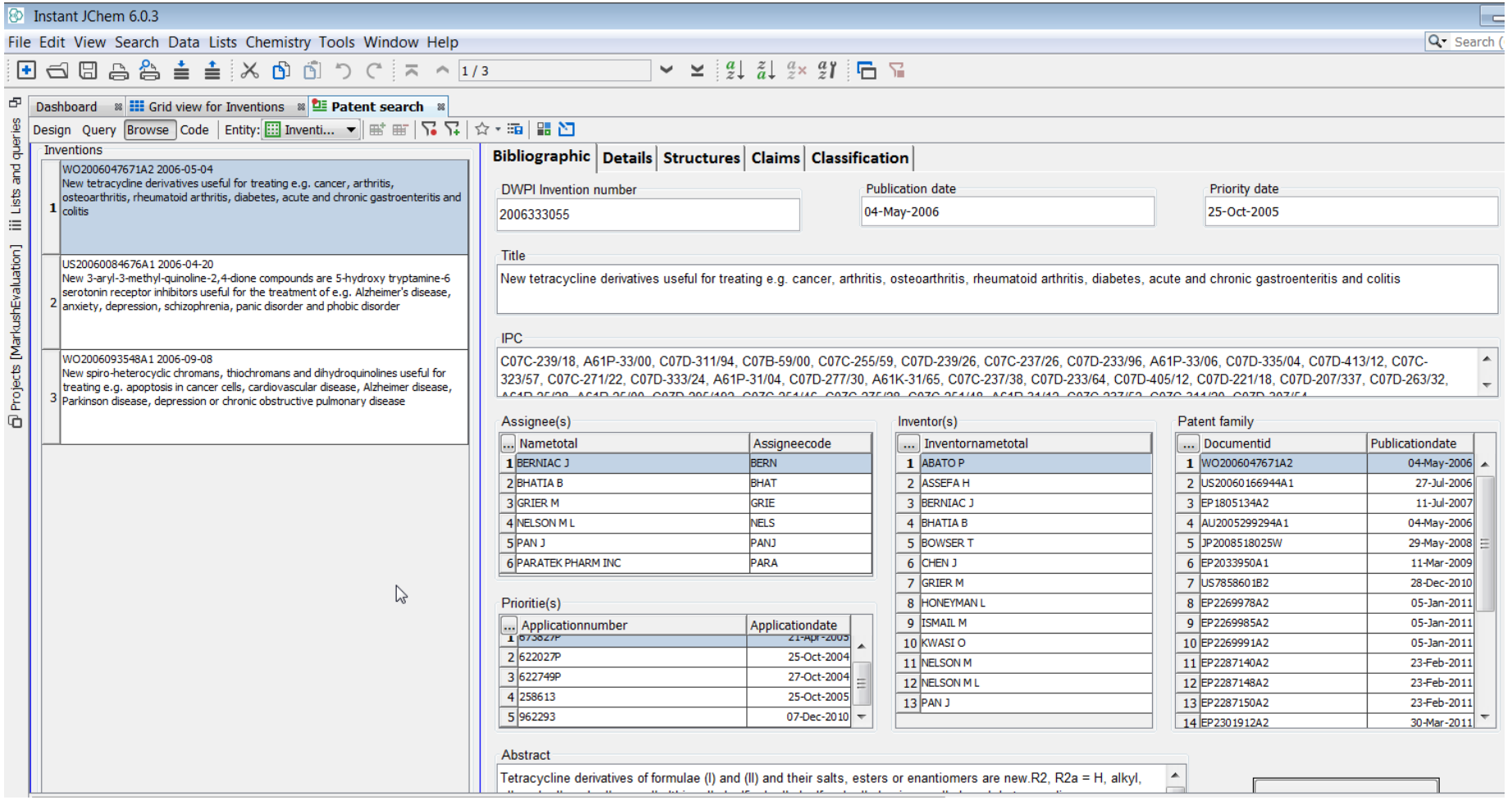
HIT PATENT (DWPI DATA)



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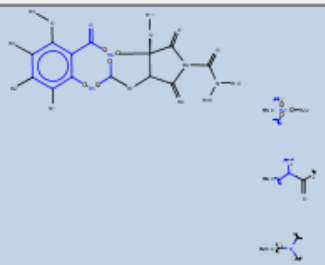
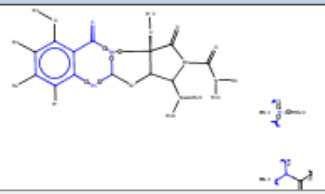
HIT STRUCTURES (MARKUSH & SPECIFIC)

Bibliographic | Details | Structures | Claims | Classification

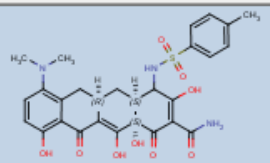
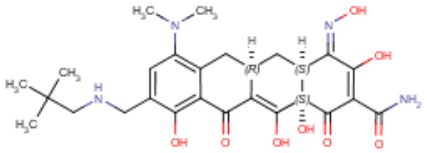
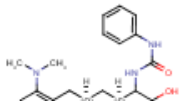
Markushes

...	Structure	DERWENTID	Compactedroles
1		032635101	N
2		032635102	N

Export All

Export selected

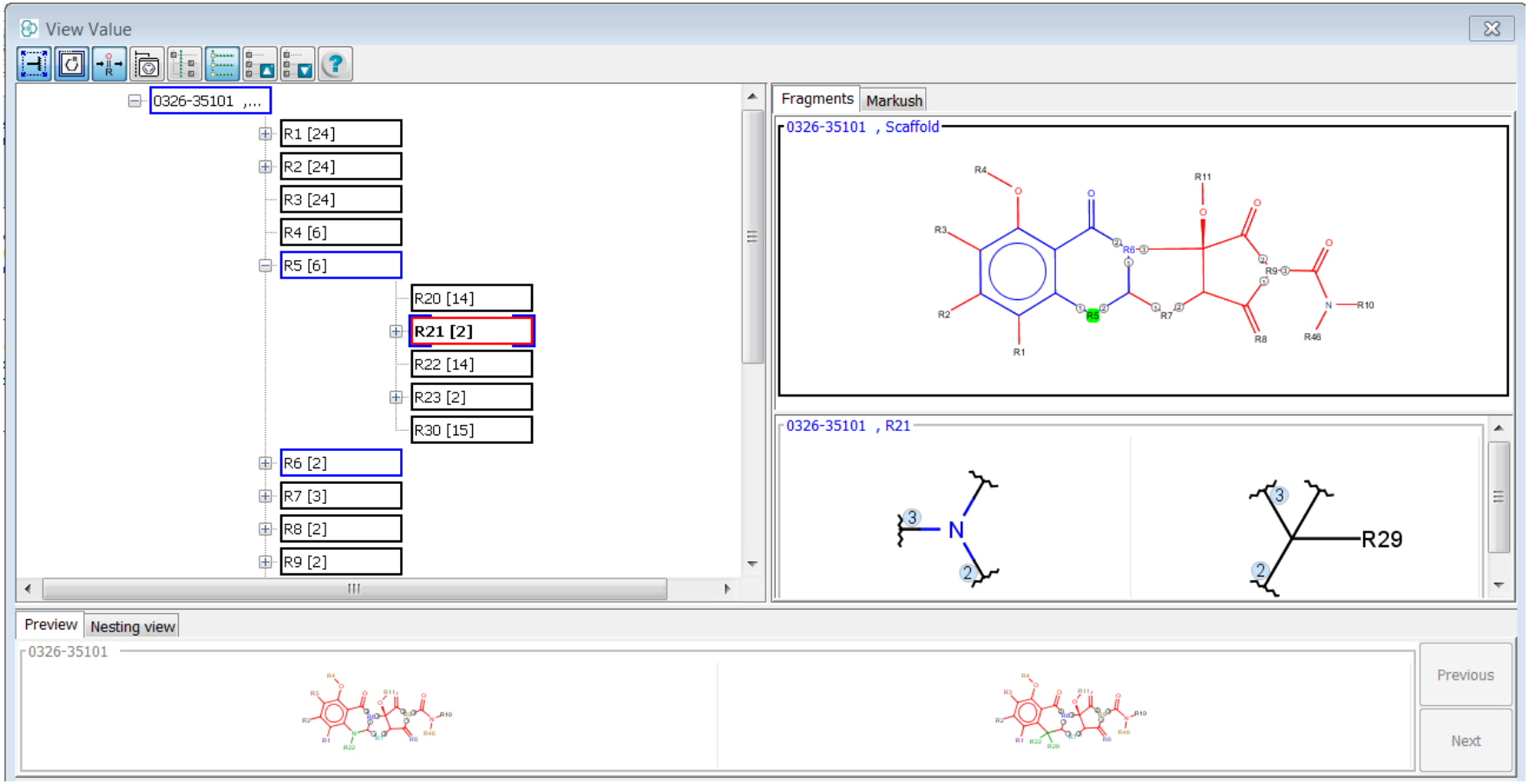
Examples

...	Structure	COMPOUNDID	Compactedroles
1		1300430	N
2		1300422	N
3		1300429	N

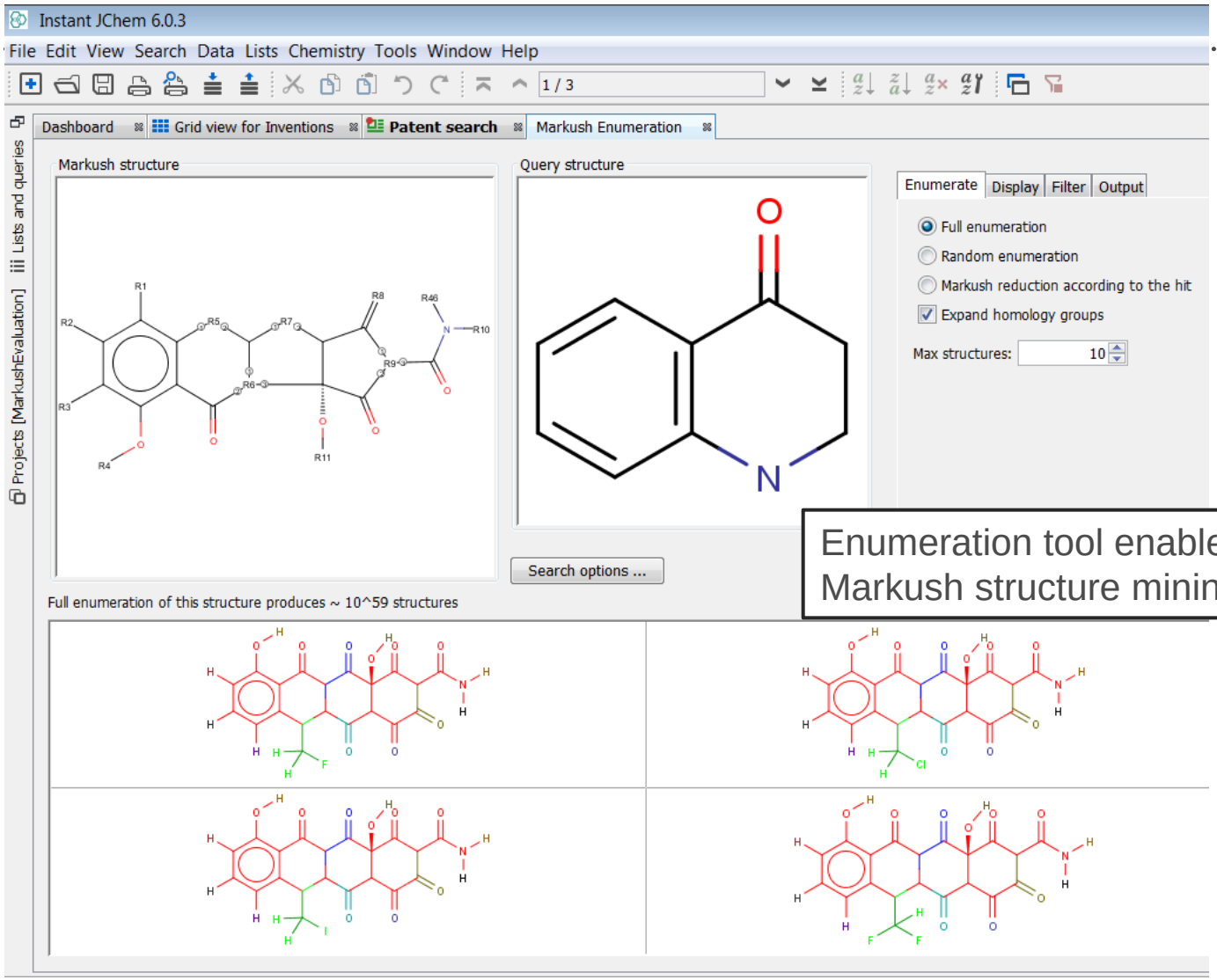
Export All

Export selected

MARKUSH VIEWER



ENUMERATION TOOL



Enumeration tool enables Markush structure mining

SUMMARY

- New cloud-hosted Markush offers comprehensive data via a powerful and convenient platform
- Markush analysis allows us to view the chemistry patent landscape
  - broad view of trends for companies, countries etc
  - narrower view for particular structure types
    - shows which companies are active, trends over time, top inventors, drug activities etc.

Thank you

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