



PASS: Prediction of Activity Spectra for Substances Twenty Years of Development Vladimir Poroikov, Dmitry Filimonov,

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Acknowledgements to the key persons



and to many other colleagues who help us in PASS development

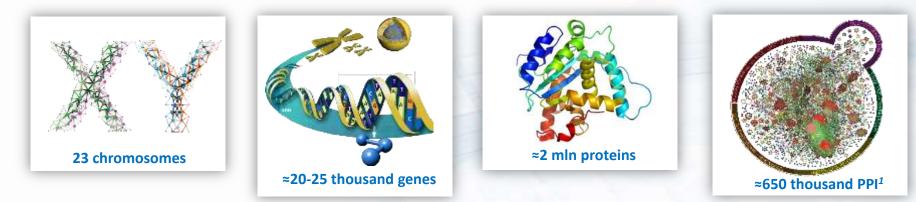


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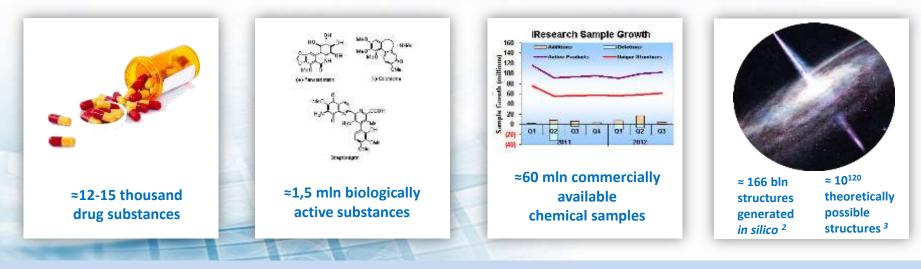
ACS Natl. Meetings	Titles of our Presentations
245th (2013)	Virtual high-throughput screening of novel pharmacological agents based on PASS predictions
239th (2010)	Fragment-based drug design using PASS approach
237th (2009)	Public molecular databases: How can their value be increased by generation of additional data <i>in silico</i>
235th (2008)	RoadMap data: New possibilities for computer-aided drug discovery
229th (2005)	Why relevant chemical information cannot be exchanged without disclosing structures
225th (2003)	Computer-aided discovery of compounds with combined mechanism of pharmacological action in large chemical databases
223th (2002)	Computer-aided prediction of activity spectra for substances (PASS)
222th (2001)	Computer-assisted mechanism-of-action analysis of large databases, including 250,000 chemical compounds registered by NCI

We are living in the time of Big biomedical and chemical Data

Potential biomarkers and pharmacological targets



Potential chemical probes and pharmaceutical substances



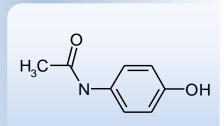
1. PNAS, 2008, 105: 6959-6964.

2. JCIM, 2012, 53: 56-65.

3. JCICS, 2003, 43: 374-380.

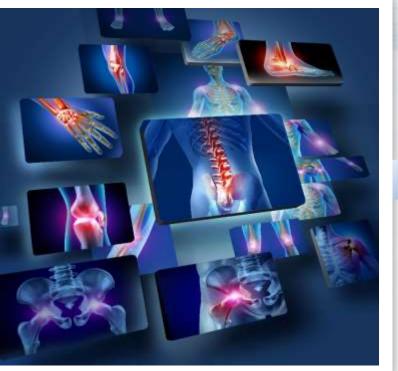
Most of pharmaceutical substances exhibit pleiotropic effects, which may become the reason:

E.g, Acetaminophen



a) For treatment of certain pathology due to the desirable actions.

b) For adverse/toxic actions caused severe disorders or even death.

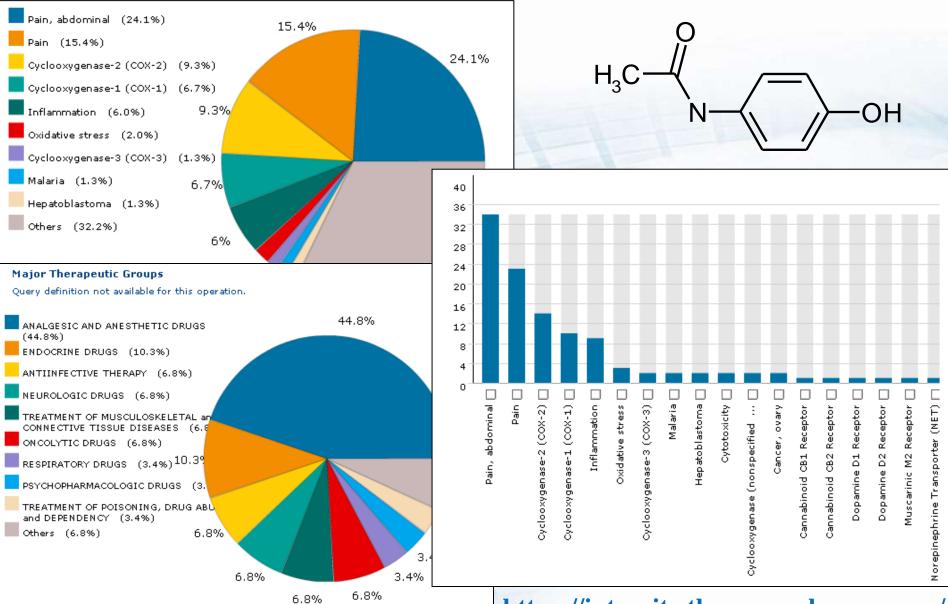


Antipyretic Analgesic NSAID Antiosteoporotic Antineoplastic COX inhibitor

Hepatotoxic



Pharmacological Studies of Acetaminophen



https://integrity.thomson-pharma.com/

To estimate the biological potential of the compound in silico, we proposed the concept of biological activity spectrum:

Biological Activity Spectrum is the intrinsic property of the compound reflected all biological activities, which can be found in the compound's interaction with biological entity.

Poroikov V.V., Filimonov D.A., Boudunova A.P. Automatic Documentation and Mathematical Linguistics. Allerton Press Inc., 1993, 27: 40-43.

Filimonov D.A., Poroikov V.V., Karaicheva E.I. et. al. *Experimental and Clinical Pharmacology*, 1995, 58: 56-62 (Rus).

Filimonov D.A., Poroikov V.V. In: *Bioactive Compound Design: Possibilities for Industrial Use*, BIOS Scientific Publishers, Oxford (UK), 1996. pp. 47-56.

Non-synonymous definitions found in literature

Lewi P.J. Spectral mapping, a technique for classifying biological activity profiles of chemical compounds. *Arzneimittelforschung*. 1976; 26 (7):1295-1300.

Battistini A. et al. **Spectrum of biological activity** of interferons. *Annali dell'Istituto Superiore di Sanità*. 1990; **26** (3-4):227-253.

Gringorten J.L. et al. Activity spectra of Bacillus thuringiensis deltaendotoxins against eight insect cell lines. *In Vitro Cell. Dev. Biol. Anim*. 1999; **35** (5):299-303.

Fliri A.F. et al. **Biological spectra** analysis: Linking **biological activity profiles** to molecular structure *Proc. Natl. Acad. Sci. USA*. 2005; **102** (2): 261–266.

Rana A. Benzothiazoles: A new **profile of biological activities**. *Indian J. Pharm. Sci.* 2007; **69**:10-17.

Fedichev P., Vinnik A. **Biological Spectra** Analysis: Linking **Biological Activity Profiles** to Molecular Toxicity. 2007; http://www.qpharm.com.

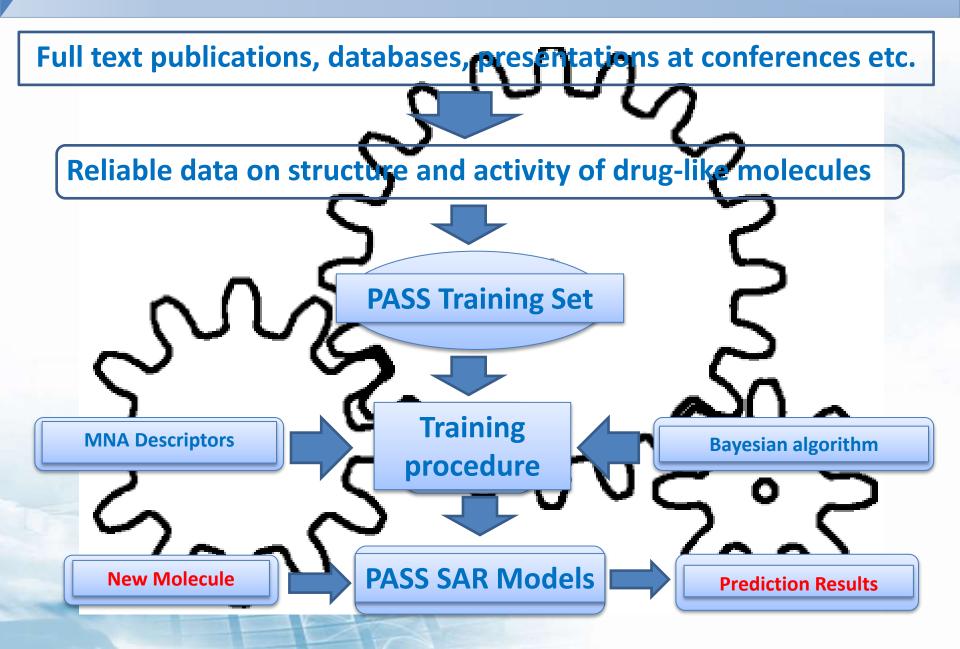
Requirements to the creating such program

Predicts many (ideally, all known) activities

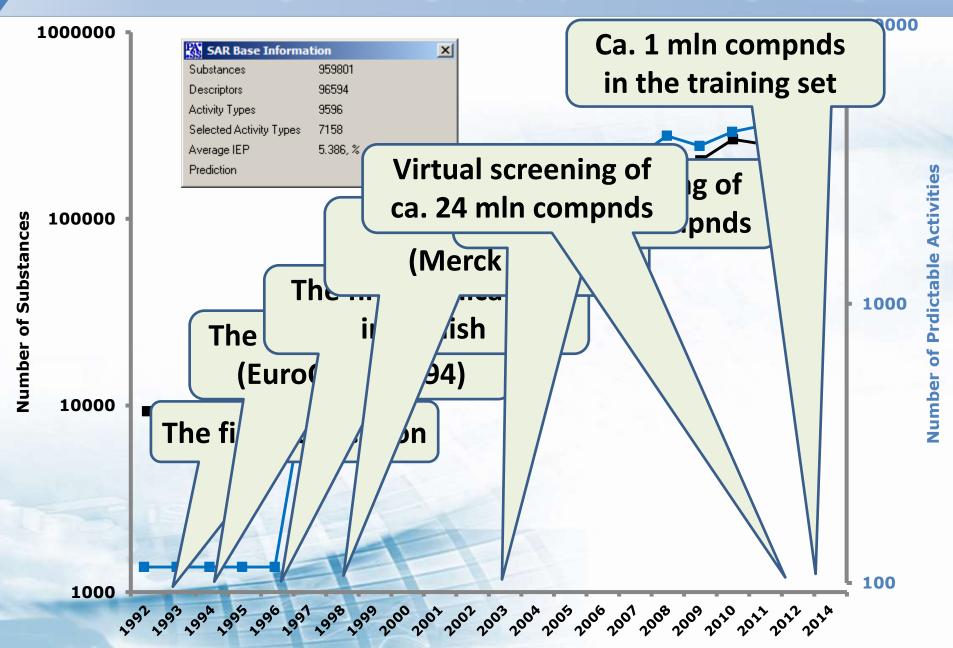
Uses only structural formula as input data (MOL or SDF)

Can be re-trained with new data sets Has user-friendly interface ("one click" to get prediction)

PASS is based on the ligand-based drug design approach



PASS training set is regularly updated and growing



PASS 2014 Characteristics

Training Set	959,801 drugs, drug-candidates, pharmacological and toxic substances comprise the training set
Biological Activity	7,158 biological activities can be predicted (Active vs. Inactive)
Chemical Structure	Multilevel Neighborhoods of Atoms (MNA) descriptors [1, 2]
Mathematical Algorithm	Bayesian approach was selected by comparison of many different methods [2]
Validation	Average accuracy of prediction in LOO CV for the whole training set is ~95% [2]; robustness was shown using principal compounds from MDDR database [3]

1. Filimonov D.A. et al. J. Chem. Inform. Computer Sci., 1999, 39, 666.

2. Filimonov D.A., Poroikov V.V. In: Chemoinformatics Approaches to Virtual Screening. RSC Publ., 2008, 182-216.

3. Poroikov V.V. et al. J. Chem. Inform. Computer Sci., 2000, 40, 1349.

Types of biological activity predicted by PASS

Main pharmacological effects

(antihypertensive, hepatoprotective, anti-inflammatory etc.);

Mechanisms of action

(5-HT1A agonist, cyclooxygenase 1 inhibitor, adenosine uptake inhibitor, etc.);

Specific toxicities

(mutagenicity, carcinogenicity, teratogenicity, etc.);

Interaction with Antitargets

(HERG channel blocker, etc.);

Metabolic terms

(CYP1A substrate, CYP3A4 inhibitor, CYP2C9 inducer, etc.);

Influence on gene expression

(APOA1 expression enhancer, NOS2 expression inhibitor, etc.);

Action on transporters

(Dopamine transporter antagonist, Sodium/bile acid cotransporter inhibitor, etc.).

Results of PASS Prediction for Clopidogrel

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5x5 4x4 3x3 2x2	Molecular Structure MNA	Antithrombotic	•
$ \begin{array}{c} 1 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0$	<pre>> <name> (0) Clopidogrel</name></pre>	Effects Mechanisms Toxicity Antitargets Metabolism Gene Exp. 45 of 464 Possible Pharmacological Effects at Pa > Pi 0.951 0.004 Neuroprotector 0.886 0.005 Acute neurologic disorders treatment 0.723 0.006 Antithrombotic 0.712 0.004 Platelet aggregation inhibitor 0.618 0.019 Antianginal 0.553 0.013 Atherosclerosis treatment 0.463 0.048 Analgesic 0.385 0.009 Platelet antagonist 0.385 0.009 Platelet antagonist 0.382 0.009 Platelet antagonist 0.383 0.027 Stroke treatment 0.352 0.026 Angiogenesis stimulant 0.322 0.013 Analgesic, opioid 0.324 0.449 Antiinflammatory, ophthalmic 0.341 0.116 Spasmolytic, urinary 0.290 0.102 Cell adhesion molecule inhibitor 0.301 0.135 Neurodegenerative diseases treatment 0.261 0.938 Antipsoriatic	
1/129	0.723 0.006 Antithrombotic		11.

Results of PASS Prediction for Clopidogrel

Abdominal pain Acute neurologic disorders treatment **Agranulocytosis Allergic reaction Anaphylaxis** Anemia Angioedema **Angiogenesis inhibitor** Antianginal Antiarthritic **Anticoagulant Antineoplastic Antipsoriatic** Antithrombotic Anxiety **Arthralgia** Atherosclerosis treatment **Back pain Behavioral disturbance** Blindness **Bronchoconstrictor** Cardiotoxic Cataract **CCL4 expression enhancer CCL5** expression enhancer **Chest pain** Colic Colitis

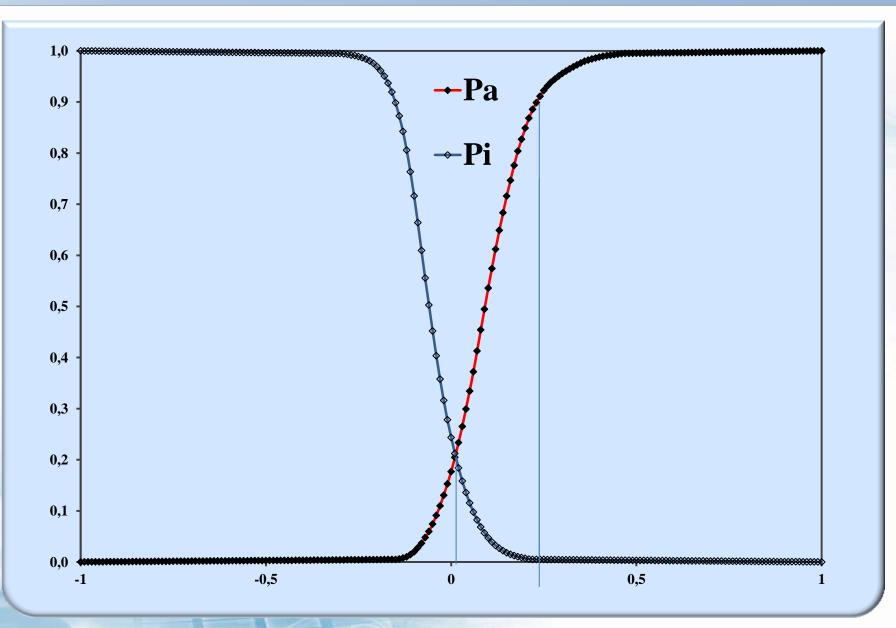
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Henoch-Schonlein purpura **Hepatic failure Hepatitis Hepatotoxic Hypertensive Hyperthermic Hypotension** Infection Insomnia Lassitude Leukopenia Lichen planus **Lichenoid eruption** Malaise Menstruation disturbance **Myalgia** Nausea Necrosis **Nephrotoxic** Neuroprotector **Neutropenia Ocular toxicity** Pain **Pancreatitis Pancytopenia Platelet aggregation inhibitor Platelet antagonist Pruritus Pulmonary embolism**

Purinergic P2 antagonist Purinergic P2T antagonist Purinergic P2Y antagonist Purinergic P2Y12 antagonist Purinergic receptor antagonist Purpura **Renal colic Reproductive dysfunction** Rhinitis Sensory disturbance Serum sickness Shock Sinusitis **Sleep disturbance Stomatitis** Syncope **THBS1 expression enhancer Thrombocytopenia** Toxic **Toxic epidermal necrolysis Toxic, gastrointestinal TP53 expression enhancer** Urticaria Vasculitis Vertigo Vision disturbance

Blue – predictions coincided with the experiment. Black – unpredictable activities. Red – unpredicted activities.

Distributions of Pa and Pi for Antineoplastic activity as functions of initial Bayesian estimates



Some publications, where PASS algorithm was described

Filimonov D.A., Poroikov V.V. (2008). Probabilistic Approach in Virtual Screening. In: *Chemoinformatics Approaches to Virtual Screening*. Alexander Varnek and Alexander Tropsha, Eds. RSC Publishing, 182-216.

Filimonov D.A., Poroikov V.V. (2006). Prediction of biological activity spectra for organic compounds. *Russian Journal of General Chemistry*, 50 (2), 66-75.

Poroikov V., Filimonov D. (2005). PASS: Prediction of Biological Activity Spectra for Substances. In: *Predictive Toxicology*. Ed. by Christoph Helma. N.Y.: Taylor & Francis, 459-478.

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Examples of PASS-based search for new biologically active compounds

J. Chem. Inf. Comput. Sci. 2003, 43, 228-236 Available online at www.sciencedirect.com BCIENCE ODIRECT Bioorganic & PASS Biological Activity Spectrum Predictions in the Enhanced Open Medicinal Chemistry NCI Database Browser **FLSEVIER** Bioorganic & Medicinal Chemistry 12 (2004) 6559-6568 Design, synthesis, computational and biological evaluation Vladimir V. Poroikov,[‡] Dmitrii A. Filimonov,[‡] Wolf-Dietrich Ihlenfeldt,[#] Tatyana A. Gloriozova,[‡] of new anxiolytics Alexey A. Lagunin,[‡] Yulia V. Borodina,[‡] Alla V. Stepanchikova,[‡] and Marc C. Nicklaus*,[†] Laboratory of Structure-Function Based Drug Design, V.N. Orekhovich Institute of Biomedical Chemistry of Athina Geronikaki,^{a,*} Eugeni Babaev,^b John Dearden,^c Wim Dehaen,^d the Russian Academy of Medical Sciences, 10 Pogodinskava Street, Moscow 119121, Russia, Computer Dmitrii Filimonov,e Irina Galaeva, Valentina Krajneva, Alexev Lagunin,e Chemistry Center and Institute for Organic Chemistry, University of Erlangen-Nümberg, Nägelsbachstrasse Fliur Macaey # Guenadiy Molodaykin f Vladimir Poroikoy e Serehei Poershnoi # Chemistry of Heterocyclic Compounds, Vol. 42, No. 5, 3006 2870 J. Med. Chem. 2004, 47, 2870-2876 Design of New Cognition Enhancers: From Computer Prediction to Synthesis SYNTHESIS AND ANTI-INFLAMMATORY and Biological Evaluation ACTIVITY OF ETHYNYLTHIAZOLES Athina A. Geronikaki,^{*,1} John C. Dearden,[‡] Dmitrii Filimonov,[§] Irina Galaeva,[#] Taissia L. Garibova,[#] Tatiana Gloriozova.⁸ Valentina Krajneva,⁸ Alexey Lagunin.⁸ Fliur Z. Macaev,¹ Guenadij Molodavkin.⁰ A. Geronikaki¹, S. Vasilevsky², D. Hadjipaviou-Litina¹, A. Lagunin, and B. V. Poroikov³ Vladimir V. Porotkov,[§] Serghei I. Pogrebnot,¹ Feltx Shepeli,¹ Tatiana A. Voronina,⁸ Maria Tsitlakidou,⁷ and Liudmila Vlad¹ A series of acetylene derivatives of thiazole using the Sonogashira cross-coupling method was School of Pharmacy, Department of Pharmaceutical Chemistry, Aristotle University of Thessaloniki, Thessaloniki, Greece, synthesized and evaluated in vivo for their anti-inflammatory activity. Four compounds exhibited good 3326 J. Med. Chem. 2003, 46, 3326-3332 anti-inflammatory activity and two inhibited saybean lipoxygenase. Computer-Aided Selection of Potential Antihypertensive Compounds with Dual Available online at www.sciencedirect.com Mechanism of Action EUROPEAN JOURNAL OF ScienceDirect MEDICINAL CHEMISTRY Alexey A. Lagunin,^{*} Oleg A. Gomazkov, Dmitrii A. Filimonov, Tatyana A. Gureeva, Elvira A. Dilakyan, ELSEVIER European Journal of Medicinal Chemistry 44 (2009) 473-481 J. Med. Chem. 2008, 51. 1601-1609 http://www.elsevier.com/locate/ejmach Original article Computer-Aided Discovery of Anti-Inflammatory Thiazolidinones with Dual Cyclooxygenase/ Evaluation of the local anaesthetic activity of 3-aminobenzo[d]isothiazole Lipoxygenase Inhibition derivatives using the rat sciatic nerve model Athina A. Geronikaki," Alexey A. Lagunin,** Dimitra I. Hadjipavlou-Litina," Phaedra T. Eleftheriou,† Dmitrii A. Filimonov, Athina Geronikaki a., Paola Vicini b, Nikos Dabarakis C, Alexey Lagunin d, Vladimir Poroikov d, Vladimir V. Poroikov,⁴ Intekhab Alam,⁸ and Anil K. Saxena⁸ John Dearden ", Hassan Modarresi ", Mark Hewitt ", George Theophilidis 1 Department of Pharmaceutical Chemistry, School of Pharmacy, Aristotle University, Theosaloniki, 54124, Greece, Institute of Bi European Journal of Medicinal Chemistry 47 (2012) 111-124 Current Pharmaceutical Design, 2010, 14, 1703-1717 Multi-Targeted Natural Products Evaluation Based on Biological Activity Prediction Contents lists available at SciVerse ScienceDirect with PASS European Journal of Medicinal Chemistry Alexey Lagunin, Dmitry Filimonov and Vladimir Poroikov* journal homepage: http://www.elsevier.com/locate/ejmech Institute of Biomedical Chemistry of Rus. Acad. Med. Sci., 10, Pogodinskaya Str., Moscow, 119121, Russia Original article Abstract: Natural products found a write use in folk medicant. Presently, when rentine development of new drugs faced a considerable

challenge, they become an inspiration and valuable source in drugs discovery. Rather complex and diverse chemical structures of natural compounds provide a bous for modulation of different biological targets. Natural compounds exhibit a analitizageted action flat may lead

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Fragment-based design, docking, synthesis, biological evaluation and

PharmaExpert: Tool for analysis of PASS prediction results

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The search for new compounds with specific therapeutic effect(s) or/and interaction with specific target(s).

repositioning

Drug

J. Med. Chem., 2004, 47(11), 2870-2876

Bioorg. Med. Chem., 2004, 12(24), 6559-6568

Pharmaceut. Chem. J., 2011, 45 (10), 605-611

Assessment of drug-drug interactions and between natural compounds components of medicinal plants.

Curr. Pharm. Des. 2010, 16(15), 1703-1717

Med. Chem. Res. 2011, 20(9), 1509-1514

Cardiovascul. Therap. Prof., 2008, 7(5), 100-104 The search for new compounds with multiple mechanisms of action

PharmaExpert

J. Med. Chem., 2003, 46(15), 3326-3332

J. Med. Chem. 2008, 51(6), 1601-1609

Search for multitargeted compounds using PharmaExpert

Antihypertensive agents, ACE and NEP inhibitors

No ID		Structure	Structure Prediction		Experiment				
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3326

J. Med. Chem. 2003, 46, 3326-3332

Computer-Aided Selection of Potential Antihypertensive Compounds with Dual Mechanism of Action

Alexey A. Lagunin,* Oleg A. Gomazkov, Dmitrii A. Filimonov, Tatyana A. Gureeva, Elvira A. Dilakyan, Elena V. Kugaevskaya, Yulia E. Elisseeva, Nina I. Solovyuva, and Vladimir V. Poroikov

Institute of Biomedical Chemistry of Russian Academy of Medical Sciences, Pogodinskoya Street, 10, Moscow 119121, Russia

Received November 8, 2002

The prediction of biological activity spectra for substances as an approach for searching compounds with complex mechanisms of action was studied. New compounds with dual mechanisms of artithypertensive action were found by this approach. Biological activity spectra for substances were predicted on the basis of their structural formulas by the computer program PASS. Thirty molecular mechanisms of action of compounds from the MDDR 99.2 database, which cause the antihypertensive effect and can be predicted by PASS, have been identified. The analysis of predictions for compounds with 15 dual antihypertensive mechanisms of action from the MDDR 99.2 database, applied to database has confirmed high accuracy of prediction. This approach was applied to databases of commercially available compounds (AsInEx and ChemBridge) and allowed us to select four substances that are potential inhibitors of angiotensin converting enzyme (ACE) and of neutral endopeptidase (NEP). At a later time, all these compounds were found to be the inhibitors of both ACE and NEP. The most potent compounds had IC₅₀ of 10⁻⁷–10⁻⁹ M for ACE and 10⁻⁵ M for NEP. New combinations of dual mechanisms of action never before found for antibilitors compounds were found to be the inhibitors of motion of the term of the NEP. The most potent compounds had IC₅₀ of 10⁻⁷–

Antiinflammatory agents, COX-1, COX-2, LOX inhibitors

anti-inflammatory (CPE)^{*a*} activity and COX/LOX^{*b*} inhibitory activity

			inhibitio	on %
compd	CPE%	COX-1	COX-2	LOX
1	57.3 ± 3.4	62.0	0.0	44.0
2	72.7 ± 6.8	25.0	6.2	51.0
3	51.1 ± 4.2	8.0	2.5	22.4
4	66.1 ± 1.2	60.0	4.5	12.5
5	69.4 ± 2.3	25.0	12.1	76.0
6	54.2 ± 2.4	31.0	6.2	25.0
7	44.5 ± 1.8	90.0	30.4	12.0
8	62.0 ± 2.5	50.0	2.1	44.2
9		0.0	0.0	

J. Med. Chem. 2000, 52, 1601-1600

1001

Computer-Aided Discovery of Anti-Inflammatory Thiazolidinones with Dual Cyclooxygenase/ Lipoxygenase Inhibition

Athina A. Geronikaki,⁷ Alexey A. Lagunin,^{4,7} Dimitra I. Hadiipavlos-Litina,⁷ Phaedra T. Eleftheriou,⁷ Dmitrii A. Filimonov,⁸ Vladimir V. Poroikov,⁴ Intekhub Alam,¹ and Anil K. Saxena⁸

Department of Pharmaceatrical Chemistry, School of Pharmace, Aristotle University, Theradoniki, 54124, Greece, Institute of Biomedical Chemistry of Russian Academy of Medical Sciences, Pergodinulaya Street, ID, Moscow, 119121, Russia, and Medicinal Chemistry Division, Control Drug Research Iomitate, Chastar Margil Palace, Luchanov 226 001, India

Received July 24, 2007

New anti-inflammatory agents possessing dual cycloaxygenuse/lipoxygenuse (COXLOX) inhibition were discovered by computer-aided prediction of biological activity for 573 virtually designed chemical compounds. Prediction of biological activity was performed by PASS, and prediction results were analyzed with PharmaExpert software. Nine 2-(thiazole-2-ylamino)-3-phenylidene-4-thiazolidinone derivatives differing by the phenyl group substitution were selected for synthesis and experimental testing as potential COXI. LOX inhibitors. Eight tested compounds exhibited anti-inflammatory activity in the carrageenin-induced providents. It was shown that seven tested compounds (66.7%) were LOX inhibitors, seven compounds were COX inhibitors (77.8%), and six tested compounds (66.7%) were dual COXI/LOX inhibitors. Analysis of lipophilicity of the compounds showed a negative correlation with inhibition of edenua formation. The binding modes of the most active compounds of this series (2-(thiazole-2-ylamino)-5-(m-chlorophenylidene)-4-thiazolidinone for COX-1 and COX-2, and 2-(thiazole-2-ylamino)-5-(m-nitrophenylidene)-4-thiazolidinone for 15-LOX were proposed on the basis of docking studies.

Finding of nootropic effect in some antihypertensive drugs based on PASS prediction



Name	Pa (Nootropic effect), %
Captopril	44,6
Enalapril	65,5
Lisinopril	61,8
Perindopril	60,9
Quinapril	65,1
Ramipril	63,3
Monopril	30,9
Piracetam	81,7
Amlodipin	-
Hydrochlorothiazide	-

BMJ Open 2013,3:e002881 doi:10.1136/bmjopen-2013-002881 Geriatric medicine

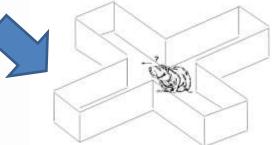
Effects of centrally acting ACE inhibitors on the rate of cognitive decline in dementia

Yang Gao^{1,2}, Rônăn O'Caoimh¹, Liam Healy¹, David M Kerins^{3,4}, Joseph Eustace⁵, Gordon Guyatt⁶, David Sammon², D William Molloy^{1,7}

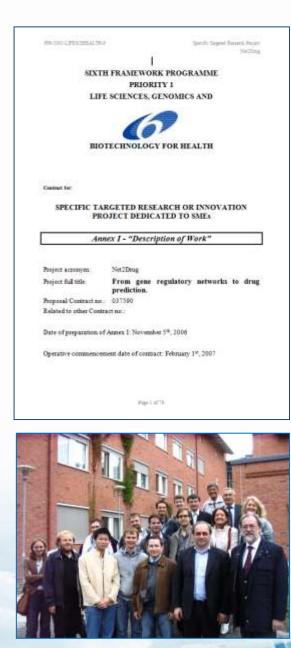
Author Affiliations

Correspondence to Professor D William Molloy, w molloy@ucc.ie Published 22 July 2013

> Perindopril in dose of 1 mg/kg, and quinapril and monopril in doses of 10 mg/kg <u>improved</u> <u>the patrolling behavior</u> in the maze, like piracetam and meclofenoxate (in doses of 300 and 120 mg/kg, respectively).

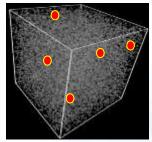


Kryzhanovskii S.A. et al. Pharmaceutical Chemistry Journal, 2012, 45: 605-611.



Participants: 9 teams from 8 countries

European project «From analysis of gene regulatory networks to drug» (Net2Drug)





Control

CAMBRIDA ASSMIRITA DOMESTA

2 active compounds

(BC, melanoma)

Synergism with RITA.

ChemNavigator database (~24,000,000 structures of organic compounds)

Virtual screening of potential multitarget anticancer substances (PASS, GUSAR)

11 compounds tested in cellular assays

Further progress:

Activity confirmed in experiments on mouse xenograft models

> ALab – resident of «Skolkovo» (2012)

Grant of «Skolkovo» (2013)

More active analogs (2014)

PASS Online Resource



Get more information about biological potential of your

compounds.

PASS Online predicts over 4000 kinds of biological activity, including pharmacological effects, mechanisms of action, toxic and adverse effects, interaction with metabolic enzymes and transporters, influence on gene expression, etc.

To obtain the predicted biological activity profile for your compound, only structural formula is necessary; thus, prediction is possible even for virtual structure designed in computer but not synthesized yet.

Accessing to PASS Online service requires a prior <u>Registration</u>, which is free but one should agree with the <u>Terms & Conditions</u> for usage of this service.

» more information

News



Meet with the members of PASS team at the 247th ACS National Meeting, Dallas, TX, USA: 35 - Combining QSAR-analysis and fragment-based drug design in search for new anti-HIV agents. (more...).



Meet with the members of PASS team at the 247th ACS National Meeting: 283 - Computer-aided study of hidden potential in Traditional Indian Medicine Ayurveda (more...)



Meet with the members of PASS team at the 247th ACS National Meeting: 229 - Prediction of activity spectra of substances (PASS): Twenty years of development. (more).

http://way2drug.com/passonline

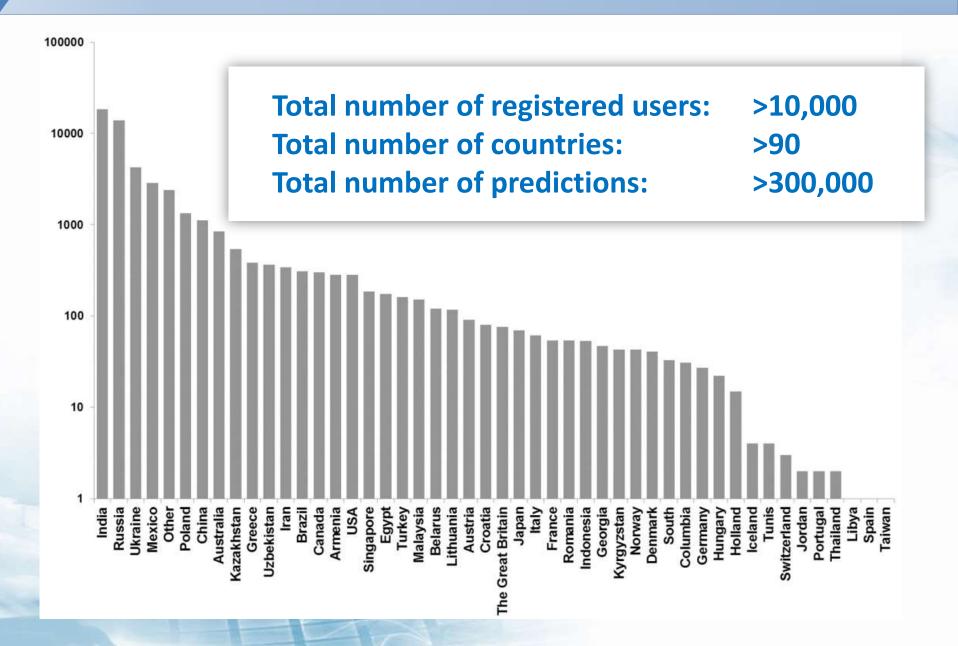
Prediction for structure presented by MOL file

» Home	» Definition » Pro	ducts >> Services	» FAQ	» Contacts
	~			
	Predict new compound	View old results	View/change r	
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Prediction Results

PASS onlin	ເ⊖ີ Vladimir Poroikov (<u>Log out) Go</u> ຂ ຊ
» Home » Definition »	Products » Services » FAQ » Contacts
Predict new compound SMILES	View old results View/change profile MOL file Marvin applet
FA	DATABASES\TEST-MOLEC
0,123 0,014 DIOIIC	noconstructor
	et aggregation inhibitor
0,733 0,034 Pain	
0,719 0,026 Hypot	ension
0,698 0,012 Catar	act
0,718 0,035 Derma	atitis
0,703 0,028 Conso	iousness alteration
0,700 0,040 Emeti	
0,697 0,038 Heada	iche
0,682 0,030 Hyper	tensive
0,650 0,004 CYP2	C19 inhibitor
0,659 0,050 Nause	×a – – – – – – – – – – – – – – – – – – –

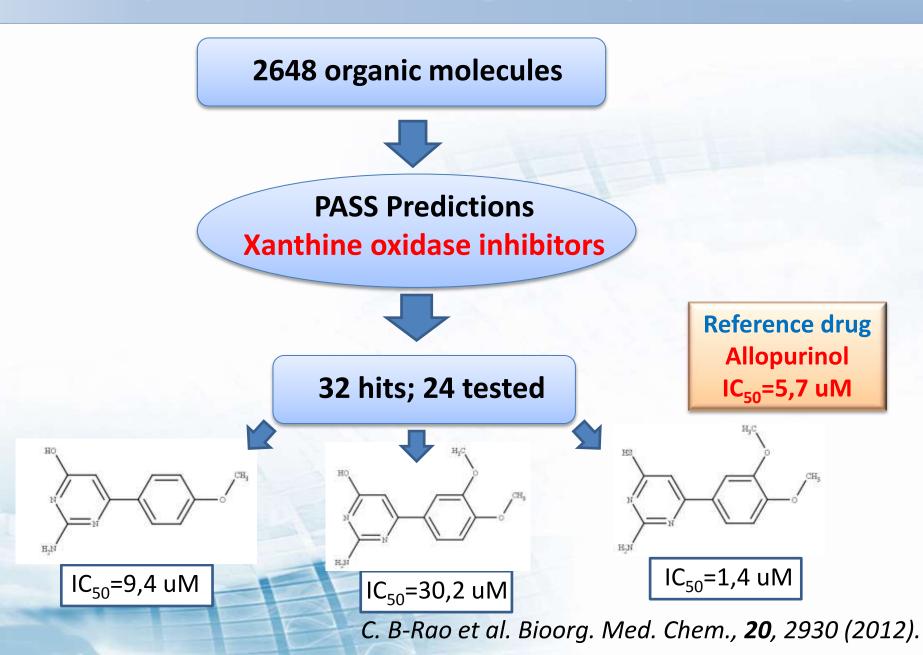
PASS Online Utilization in 2013



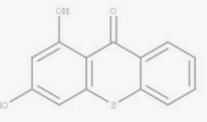
Over 150 independent publications with PASS online predictions (>50% papers with experimental testing of prediction results)

0.000	Available online at www.sciencedrect.com		Available online at www.sciencedirect.com Bioorgan Bioorganic & Medicinal Chemistry Letters 15 (2005) 2145-2148 Bioorganic & Medicinal Chemistry Letters 15 (2005) 2145-2148 Bioorgani	al
ANTMICROBIAL AG 0066-4804/03/508.00 Copyright © 2003, /	In Vitro Activities of 7-Substituted 9-Chloro and ino-2-Methoxyacridines and Their Bis- and Tetra- Complexes against <i>Leishmania infantum</i>		and GADACIGIC agcins	E.V. <mark>T</mark> ret'ya 2, pp. 230–2
Chemistry of Het A DRUG M MOLECUL	i Giorgio, ^{1*} Florence Delmas, ¹ Nathalie Filloux, ² Maxime Robin, ² Laeti nerocyclic Compounds, Vol. 49, No. 1, April, 2013 (Russian Original Vol. 49, No. 1, January, IVSTERY OF HETEROCYCLES: VARIOUS LES FOR ONE TARGET OR ONE COMPOUND IIPLE TARGETS? Biorgane & Medicad Chemistry 20 (2012) 2020-2020		 Structure, and Pharmacological Activity Epoxy-(13R,17R)-trioxolane Abietic Acid Smirnova^a, H. Do Tkhi Tkhu^b, Tkhankh Tra Nguen^b, G. N. Apry V.I. Zvarych, R.Ya. Musyanovych, V.G C 	yshko ^c , DC 547.67
FI SPVIFR	Contents lists available at SciVerse ScienceDirect Bioorganic & Medicinal Chemistry journal homepage: www.elsevier.com/locate/bmc	SYI	O.Z. Komarovska-Porokhnyavets, M.V. Stasevych, V Lviv Polytechnic Nationa Department of Technology of Biologically Active Pharmacy and Bi NTHESIS OF NEW DERIVATIVES OF 2-ACYLISOTHIOCYAN	al Universi Substance iotechnolog
	n of novel isocytosine derivatives as xanthine oxidase om a set of virtual screening hits European Journal of Medicinal Chemistry 45 (2010) 2006–2012 Contents lists available at ScienceDirect European Journal of Medicinal Chemist	удк 378.147:: Комбин	⁵⁴⁷ іаторная химия в высшей школе: десятилетний опыт науч учебных и организационных проектов Е.В. Бабаев	чных,
- The Your State				

Example 1. Virtual screening of the synthetic library



Example 2. Prediction of the most probable activities of xantones and thioxantones for testing *in vitro*



Activity	Pa	Pi
Antinourotovio	0.850	0.005

The only activities that were tested are antimicrobial (S. aureus, S. pneumonia, S. pyogenes, M. catarrgalis, H. influenza, E. Coli) and cyrotoxic (HepG2 and Jurkat cell lines). No such activities were predicted and found experimentally).

Verbanac D. et al. Bioorg. Med. Chem., 20, 3180 (2012)

	Quercetin 2,3-dioxygenase inhibitor	0,543	0,005
2	Thioredoxin disulfide reductase inhibitor	0,541	0,007
20	FMO3 substrate	0,540	0,008
C	CF transmembrane conductance regulator inhibitor	0,539	0,005
Q	Sulfotransferase substrate	0,505	0,004
S	Estrogen beta receptor agonist	0,501	0,001

Example 3. Prediction of the most probable activities of pyranopyrazole derivatives for testing *in vivo*

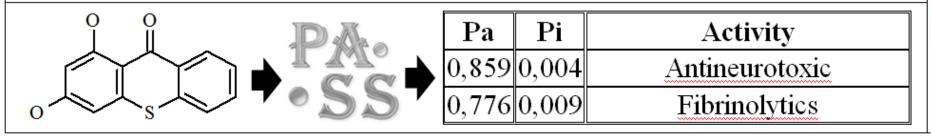
Analgesic and anti-inflammatory activity of these compounds was shown on experimental models in mice. Using docking the authors concluded that COX-2 inhibiting activity reduces in the following order: phenothiazolyl > benzothiazolyl > quinolyl> pyridiminyl > OCH₃ > Br > CH₃ > H. However, these conclusions require experimental verification. Kumar A. et al. Eur. J. Med. Chem., 50, 81 (2012)

Complement factor D inhibitor	0,572	0,050
Immunomodulator	0,532	0,033
Immunosuppressant	0,454	0,044
Cyclooxygenase inhibitor	0,400	0,004
HCV IRES inhibitor	0,431	0,050

Systematic review of these >150 publications is accepted for publication by "Chemistry of Heterocyclic Compounds"

■Graphical abstract

D. A. Filimonov, A. A. Lagunin, T. A. Gloriozova, A. V. Rudik, D. S. Druzhilovsky, P. V. Pogodin, V. V. Poroikov Prediction of biological activity of organic compounds using web-resource PASS Online



Filimonov D.A. et al. Chemistry of Heterocyclic Compounds, No. 4 (2014).



In December 2013 we executed an interview of active PASS Online users

Please, fill in the Anonymous form below.

1. Where are you working?

Academy (University)

Research Institute

Industry

Regulatory Agency

Other (Please, specify)

2. What is your field of activity?

Organic Chemistry

Medicinal Chemistry

Pharmacology

Toxicology

Pharmacy

Other (Please, specify)

3. What is your primary aim to use PASS Online service?

Planning of Chemical Synthesis

Planning of Biological Testing

Finding New Actions of Known Compounds

Chemical Safety & Risk Assessment

Other (Please, specify)

4. How satisfied are you by PASS Online service?

Very Sat. means that you are very satisfied by this aspect of PASS Online service. Sat. means that you are satisfied by this aspect of PASS Online service. N. means that you can't decide whether you are satisfied by this aspect of PASS Online service. Dissat, means that you are dissatisfied by this aspect of PASS Online service. Very Dissat, means that you are very dissatisfied by this aspect of PASS Online service.

On PASS Online service how I feel about	Very				Very
	Dissat.	Dissat.	Ν.	Sat.	Sat.
Registration procedure					
Structure input					
Accessibility via Internet					
User interface					
Speed of response					
List of predictable activities					
Results of prediction					

5. To improve PASS Online service are you ready...

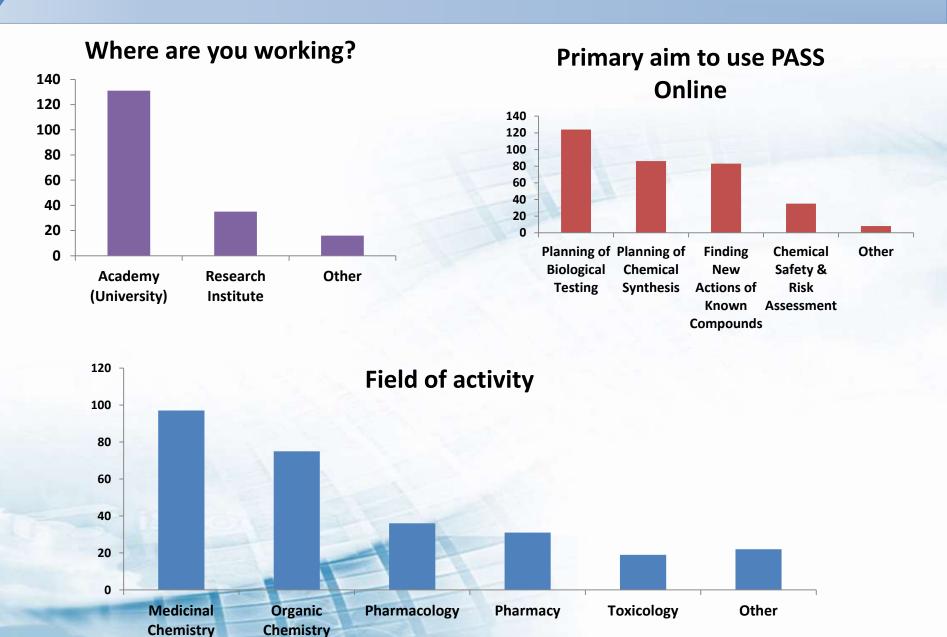
Very Likely means that you will very likely to take part in this activity. Likely means that you will likely to take part in this activity. N. means that you can't decide whether you will take part in this activity or not. Unlikely means that you will unlikely to take part in this activity. Very Unlikely means that you will very unlikely to take part in this activity.

I am ready	Very Unlikely	Unlikely	Ν.	Likely	Very Likely
To submit a feedback about correspondence of predictions with the experiment					
To submit the proposal what can be done for improvement of PASS Online					
To submit the proposal which biological activities should be covered by PASS Online					
To submit the proposal which chemical series should be covered by PASS Online					
Take part in a joint work to input data on active compounds from particular chemical series to update PASS Online training set	_	_	_	_	_
To refer on PASS Online prediction results in					Ц
my publications To recommend PASS Online service to other					
colleagues					

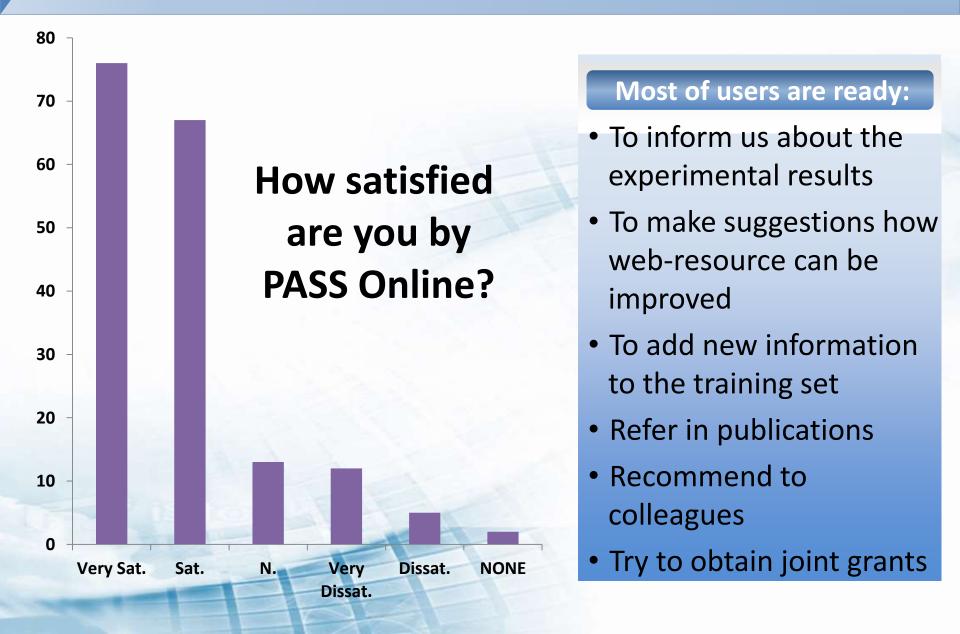
6. Are you willing to share some information about your activity, to find some partners for collaborative projects?

Very Likely means that you will very likely to take part in this activity. Likely means that you will likely to take part in this activity. N. means that you can't decide whether you will take part in this activity or not. Unlikely means that you will unlikely to take part in this activity. Very Unlikely means that you will very unlikely to take part in this activity.

Responses on the questions (1)



Responses on the questions (2)



Major comments of the users

- 1. Acknowledgements etc.
- 2. Collaboration
- 3. Interface, general remarks
- 4. Presentation of the prediction results
- 5. Input of data
- 6. Training set
- 7. List of activities
- 8. Miscellaneous

Summary

- 1. PASS provides information about most probable biological activities based on structural formulae of organic compounds.
- 2. PASS predictions can be used for planning of synthesis and biological testing.
- 3. PASS Online is widely used by organic and medicinal chemists, pharmacologists etc.
- 4. Recommendations of PASS Online users provided during the interview can be used for further improvement of the web-resource.
- 5. PASS Online web-resource may become a platform for many collaborative projects in the field of drug discovery.



Thanks for your kind attention!

Visit our web-page: www.way2drug.com/passonline

Your questions, pls., address to: vladimir.poroikov@ibmc.msk.ru

20th EuroQSAR Understanding Chemical-Biological Interactions

20-th European Symposium on Quantitative Structure-Activity Relationships

Saint-Petersburg, Russia August 31 – September 4, 2014