



Dear ,

ACD/Labs is pleased to present our latest PhysChem/Medicinal Chemistry newsletter highlighting the 3rd Annual PhysChem Forum Symposium in the UK; a presentation from the Spring ACS meeting; results from the PhysChem Challenge; and much more.

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The Rule-of-5 Revisited

The Rule-of-5 (Ro5) has been widely adopted in the drug discovery industry (has similar equivalents in the agrochemical world) and continues to be refined and adapted, yielding several variants. This rule of thumb is used as a first step in drug discovery to quickly eliminate lead candidates with poor bioavailability properties. One of the key parameters of the Ro5 is $\log P$ —a useful descriptor but one that fails to take into account the impact on lipophilicity of varying concentrations of ionic species in biological systems. At ACD/Labs we compared application of the Ro5 using $\log D$ in place of $\log P$ on 9 commercial compound libraries.



Look out for the August issue of 'Molecular Pharmaceutics' in which we discuss the results of our study, or [read the abstract](#) now.

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Predictive Software Complements Experimental Determination

Emily Freeman is a member of the PhysChem Measurements group at UCB (Slough, UK) that measures permeability, solubility, and lipophilicity for new



chemical entities in early drug discovery. At the 3rd Annual PhysChem Forum Symposium earlier this summer, Emily presented the high-throughput method used in her group for determination of aqueous solubility and approximation of pK_a , and methods for measurement of $\log D$. She also shared the PhysChem reports that provide chemists with at-a-glance summaries, including predicted values for pK_a , polar surface area, and number of hydrogen bond donors and acceptors using ACD/Labs' software. ACD/Labs'

predictions are used to support the efforts of the PhysChem group and allows them to provide other scientists with additional property data that is not experimentally determined in-house.

[View Emily's presentation.](#)

Read other interesting presentations from the Symposium—[visit the PhysChem Forum.](#)

The speaker list included scientists from **Novartis**, **GSK**, **AstraZeneca**, **Bayer**, and **Organon**. Topics varied from practical methods for the measurement of physical properties to the use of computational methods to extend property knowledge from known compounds to related analogs.

Exploitation of PhysChem Properties in Medicinal Chemistry

Medicinal chemists are required to be mindful of the physicochemical properties of compounds they produce. In smaller biotech's and research laboratories this can be an informal process, while in large Pharma, a list of set requirements is often provided per project/target. Although the work of Lipinski and others in the field has contributed greatly to our awareness of physicochemical properties and their influence on physiological endpoints, our mastery of this subject remains incomplete. At the ACS Spring meeting we discussed topics in this area, with relevant pharmaceutical case studies:

- The importance of physicochemical properties in **medicinal chemistry**
- The commonly misunderstood concepts of **logP** and **logD**
- Effective application of PhysChem data in **lead optimization**

[View](#) the presentation.

Results of the PhysChem Challenge Are In...

After having the quiz posted on our website for a year, we decided to analyze the results to see what could be learned about our understanding of PhysChem concepts.



If you want to try it and haven't done so already, now's your chance! [Try the quiz.](#)

Of the **572 people** who took the quiz, the average score was **3/6 (50%)**. Duplicate and triplicate results of those who tried over and over again for the perfect score were removed...you know who you are.

- Top two correct answers were #4 and #5—It seems the majority of us know the difference between **logP** and **logD** (fantastic); and since aqueous solubility is a common problem, especially in drug discovery, it was gratifying that most of us know that ionization and lipophilicity both influence this property.
- Top two wrong answers were #1 and #2—'logP' and 'lipophilicity' are terms learned in undergraduate studies but knowing the theoretical definitions and understanding how a property can influence the final product and its action is different altogether. Apparently this connection of theory to practical use is missing in our repertoire.

Ranking compounds for any property is a challenge when structures

differ significantly, this is much more easily done for analogous substances. The problem is magnified when ionizable groups are added into the mix especially since $\log P$ pertains to neutral species. Question 2 was a perfect example of $\log P$ vs. $\log D$.

- Only 7 people got a **perfect score** of 6/6 (1%).

ACD/LogP Freeware—3544 Downloads and Counting...

You must have been taking a well-deserved break on a remote island if you haven't heard about this yet! At the ACS Spring meeting in Chicago, we announced the release of [ACD/LogP Freeware](#). This add-on to our drawing package, [ACD/ChemSketch](#), gives you easy access to predictions of the octanol/water partition coefficient (also referred to as ' $\log P$ ' or ' K_{ow} ').



Our calculations are based on an experimental data set of over 18,000 reliable $\log P$ measurements, and the algorithm has been continually enhanced since its introduction in 1995.

[Try it out for yourself.](#)

ACD/Labs at ACS Fall—See a Demo of Our Software

As always, ACD/Labs will be at the ACS Spring meeting in Boston at the end of August. If you are planning to attend, come to **booth #1026** in the exhibition hall (Mon–Wed) to discuss how our solutions can aid your research, and see a **demonstration of the software**. See our full [ACS Activities Schedule](#) to plan time for our oral and poster presentations. We look forward to seeing you there!

News

NMR for Everyone—Manchester University Provides Access to Industry—Leading Software
August 8, 2007 [Read](#)

How Natural Product Research Benefits from Computer Assisted Structure Elucidation
July 26, 2007 [Read](#)

Big Solutions for Small Companies: ACD/Labs Software Shortens the Path to Marketplace Success
July 23, 2007 [Read](#)

Upcoming Events

234th ACS National Meeting & Exposition 2007

Boston, MA, USA
August 19–23, 2007
Booth #1026

2007 AAPS Annual Meeting and Exposition

San Diego, CA, USA
November 11–15, 2007
Booth #2700

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