xPharm: A Preclinical Information Portal for Discovery Researchers in Institutions of Higher Learning

Marie K. Saimbert

ABSTRACT. The preclinical or discovery phase of drug development involves researchers from biologists to medicinal chemists to pharmacologists employing often unique information resources, such as xPharm. This product was developed by Elsevier MDL. The xPharm database

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purports to be a one-stop-shopping place for scientists involved in drug discovery. xPharm is a collection of original summary articles on pharmacology by scientists for scientists on pharmacologic agents or compounds, but also links related information such as agent-biological target interactions, principles supporting agent-target relationships, and disorders for which an agent may be used. This column reviews xPharm content and its possible role in the drug discovery phase, as well as where xPharm is headed in the future. A researcher is interviewed to illustrate how xPharm is used or perceived by non-librarians. A select, annotated list of other fee-based drug development databases/products and some free Internet resources can be found in the Drug Research & Development Intelligence Kit located in the Appendix of this article.

KEYWORDS. xPharm, phases of drug development, drug development, discovery, pre-clinical, agents, targets, compounds, assay, mechanism of action, pharmacology

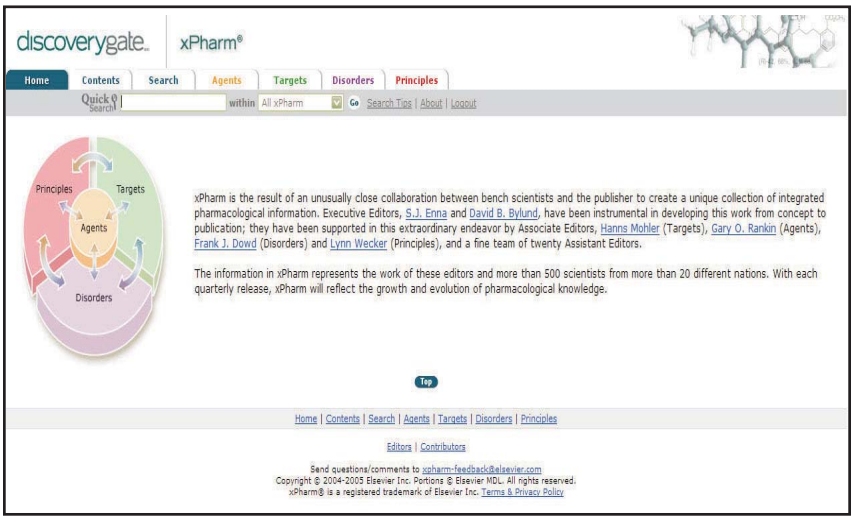
INTRODUCTION

The Preclinical or Discovery phase of drug development involves researchers from biologists to medicinal chemists to pharmacologists employing often unique information resources, such as Prous Integrity, R & D (Research & Development) Insight *(ADIS International)*, and now xPharm (*Elsevier MDL*). xPharm was developed by Elsevier MDL and released in Spring of 2003. The xPharm database, hosted on Elsevier MDL's DiscoveryGate platform, purports to be a one-stop-shopping place for scientists gathering an overview of pharmacological information in the initial phase of drug discovery–the preclinical area. xPharm is a collection of original summary articles on pharmacology by scientists, for scientists, on pharmacologic agents or compounds, but also links related information such as agent-biological target interactions, principles supporting agent-target relationships, and disorders for which an agent may be used. (A pharmacological agent can be a compound or drug that acts on a biological system or target. For instance, thiazide diuretic agents like hydrochlorothiazide target sodium chloride

transporters in the kidney's distal convoluted tubule in the body for the disorder hypertension. The xPharm agent document for hydrochlorothiazide would most likely include links to a summary on principles involved in hypertension.) This column reviews xPharm content and its possible role in the drug discovery phase, as well as where xPharm is headed in the future. Researchers are interviewed to illustrate how xPharm is used or perceived by non-librarians. A select annotated list of other fee-based drug development databases/products and some free Internet resources can be found in the Drug Research & Development Intelligence Kit located in the Appendix of this article.

xPharm is a unique product in that at least 500 scientists from over 20 nations have contributed to it, shedding light on pharmacologic targets that they research (see Figure 1). Other researchers can view the work by a previous researcher on a target and continue beyond that point. This should result in less duplication of research and may even highlight some research parameters or potential pitfalls. Original research documentation not published elsewhere appears in some xPharm monographs. Documents include unpublished electrocardiogram strips, original figures, diagrams, charts, algorithms, and slides. An example is a Suzanne Laychock's Principles summary entitled "The Pancreas and

FIGURE 1. Initial xPharm Screen–User Perspective



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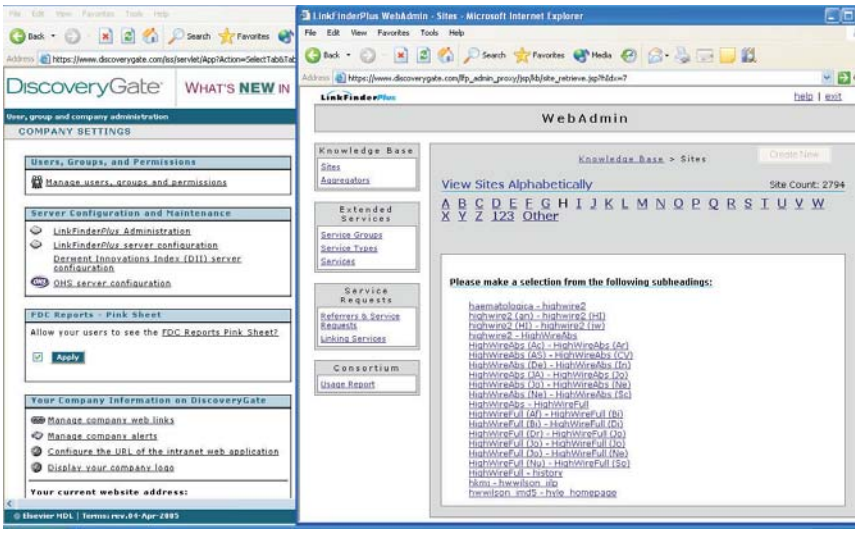
Pancreatic Hormones," which includes original drawings/figures to highlight points in her section.

Primary xPharm documents contain links to other relational data such as a Principles or Agents section. xPharm utilizes the linking capabilities on DiscoveryGate for URL compliancy, and online library articles can be linked to full-text listings in the product. Further, the DiscoveryGate platform, which holds xPharm, can be customized by libraries to include links to other database subscriptions such as *Micromedex* (Thomson Micromedex), *Physician's Desk Reference* (Thomson PDR), and *Harrison's Principles of Internal Medicine* (AccessMedicine), as shown in Figure 2. Further, access to specific records in a database is possible if the record link is included in the xPharm summary. Lastly, links to World Wide Web resources may also be found in an xPharm summary article.

KEY FEATURES OF xPharm ARTICLES

An author-affiliation hyperlink allows users to track down xPharm article authors for potential research collaboration, guest speaker engagements, and continuing education opportunities, as well as identifies

FIGURE 2. xPharm Behind-the-Scenes–Librarian Customization View



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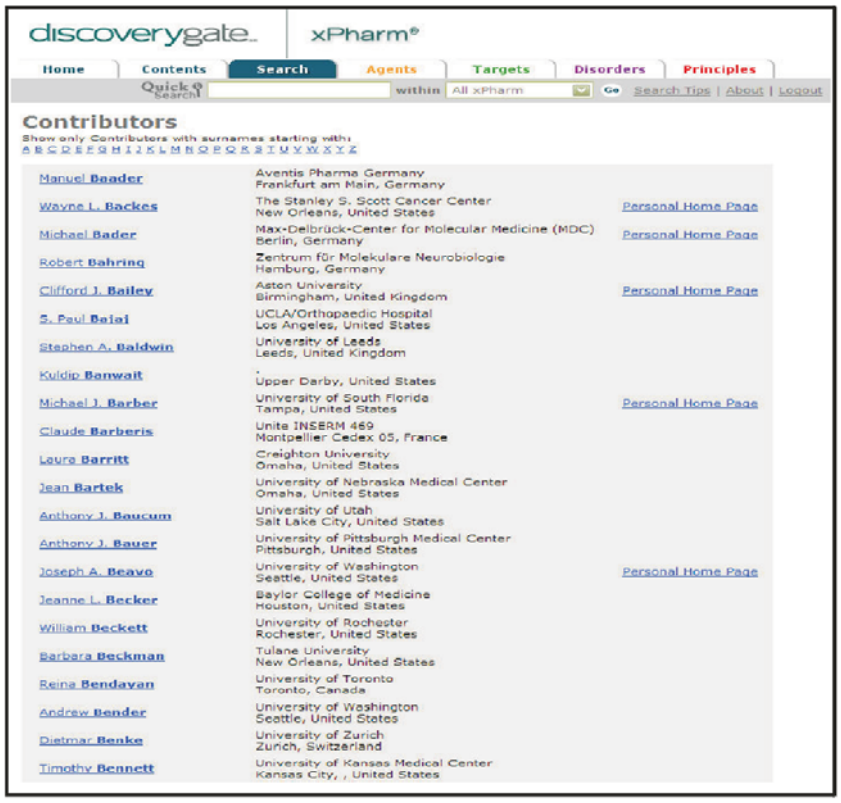
top and/or prolific researchers in a specific area. Sometimes the author link leads users to the contributor's personal Web site, where other resource links on pharmacology can be located (see Figure 3). A PDF on Pharmacology Careers from ASPET (American Society for Pharmacology and Experimental Therapeutics) is an example of one such resource.

SEARCHING xPharm BY CONTENTS

xPharm can be searched by browsing through the "Contents" tab, similar to searching the Table of Contents of an electronic book, as may

FIGURE 3. xPharm Contributor Affiliation Links



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be seen in Figure 4, and requires some subject knowledge. The Contents area appears in the left frame of the page and reveals a hierarchy of four color coded folders on agents, targets, disorders, and principles.

Orange Is for Agents

The Agents section expands by 10% to 15% yearly. Users should keep in mind that the entire xPharm database is updated quarterly. It appears up-to-date, including new agents such as lenalidomide (Revlimid), an innovative drug for multiple myeloma from the company Celgene.

Green Is for Targets

Target records, representing roughly 250 biological targets known to date, are updated most frequently. Targets included are those where target function is known. Target data includes human, rat, mouse, and other target species investigated.

Purple Is for Disorders

The Disorders section is fairly detailed. A Quick Search using the term *lupus* and the drop-down category of "Disorders" revealed an article by

FIGURE 4. Example of xPharm Record (Contents Tab Shows on Left)

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researcher Roselyn Cerutis titled, "Systemic Lupus Erythematosus." Disorders articles often include the Classification and Associated Disorders of a condition. Cause or etiology information for a disorder is comprehensive. For example, a UMDNJ user once asked if lupus could be caused by a trauma. According to the Lupus Disorders article in xPharm, one can deduce that a trauma or environmental stressor *may* contribute to activation of lupus, but is not likely to be the sole cause. Also under Etiology are receptors, chromosome, and gene data related to the Disorder. The Epidemiology section is noteworthy because it can include disorder prevalence in the United States and sometimes Europe.

Red Is for Principles

This section reveals monographs on the 180 pharmacologic principles known to date. It does not appear to be updated often, as principles do not change much and discoveries of new principles are infrequent. Content in the Principles section is perfect for pharmacology lecturers. Examples of Principle articles include "Use of Animal Models for Drug Discovery," "The Drug Approval Process in the USA," and "Pharmacodynamics."

SEARCHING xPharm BY TABS

Unlike the Contents tab search, which works best if a user possesses some subject knowledge, searching by other xPharm tabs requires use of keywords. Subject knowledge is still helpful here, but not required. The producers of xPharm recommend that users place one term or phrase in a search box. For example, typing in *dopamine receptor* using the search box within the Targets tab retrieves results that have already incorporated a wildcard feature, e.g., dopamine receptor, dopamine receptors. Typing "*dopamine receptor*" retrieves results specifically employing the quoted term and turns off the wildcard feature. (Basically, a wildcard is appended to a term/phrase placed in an xPharm search box *if* the term isn't enclosed in quotes.) At least three search boxes are offered under a search tab. An advanced search tab entitled "Search" allows users to search Agents, Targets, Disorders, and Principles. Alternatively, users can begin an Agents, Targets, Disorders, or Principles search by clicking on the respective tabs for each located next to the Search tab.

All of the search screens that are found under the respective tabs are slightly different. The Principles tab appears least detailed, offering

three search boxes for terms and operators AND, OR, or NOT. The Disorders tab includes all the detail of the Principles tab plus three distinctions: a check box for including Principles related to the search term; limits allowing search terms to be located in any of four fields of a record or a sub-field; and same field/sub-field choices for display of results, as shown in Figure 5. Note the fields and subfield choices offered for displaying results from a Disorders tab search are options available only if users do not checkmark the box to search for Principles associated with their Disorder term.

The Targets search tab offers some unique fields/sub-fields for narrowing a search term and/or result display. Again users have the option of including Principles associated with their Target search term. If users check off the Principles box in the Targets search area, fields/sub-fields highlighted above are grayed out, indicating users can no longer choose a Display format using those Target fields. Lastly, the Agents tab exhibits a similar look and functionality to the Targets and Disorders sections except for different field/subfield options for limiting search results.

FIGURE 5. Comparison of xPharm Agents–Principles Tab Search Fields

Agents	Targets	Disorders
Record Name	Record Name	Record Name
Description • Introduction • Nomenclature • Basic Chemistry	Properties • Nomenclature • Target Structure • Localization • Ligands, Substrates, Ions • Effectors, Products • Endogenous Regulation • Physiological Function	Properties • Introduction • Definition • Classification • Consequences • Associated Disorders • Etiology • Epidemiology • Pathophysiology • Signs and Symptoms
Human Pharmacokinetics	Pharmacological Regulation • Antagonist/Activator/Substrate • Antagonist/Inhibitor • Receptor Plasticity • Allosteric Regulation	Agents • Standard Therapies • Experimental Therapies • Animal Models
Targets/Pharmacodynamics	Research Tools	
Therapeutics • Indications • Contraindications • Adverse Effects • Agent-Agent Interactions	Disorders	
Preclinical Research • Other Research Information		
Other Information • Web sites • Further Reading	Other Information • Web sites • Further Reading	Other Information • Web sites • Further Reading

xPharm QUICK SEARCH OPTION

The xPharm Quick Search box is located under the xPharm folder tabs on its page. Similar to a Google search, it locates hits by weighting the term(s) entered in the search box. Users may perform a Quick Search for "All xPharm" content or choose Agents, Targets, Disorders, or Principles from the drop-down menu. If "all xPharm" content is searched, results are preceded by a colored rectangle indicating whether the primary document represents a Disorder, Agent, Target, or Principle.

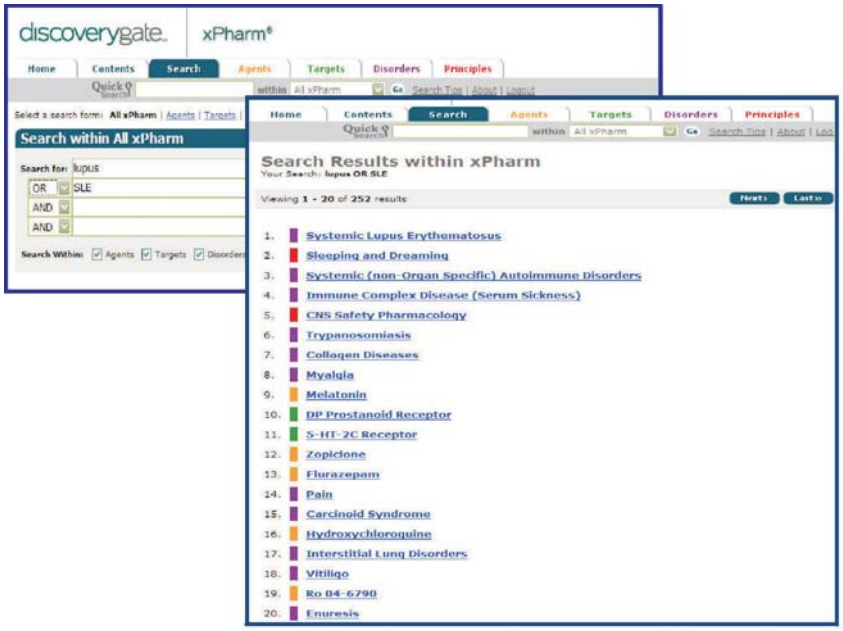
THE MAIN xPharm SEARCH BOX

The main xPharm Search Box has similar functionality to the Quick Search feature. The system is not case-sensitive, so upper or lower case alphabet can be typed. In both Quick Search and xPharm tab searches (Search, Agents, Targets, Disorders, Principles), placing a term in quotes retrieves an exact match, while terms not enclosed in quotes expand a search to variations of a typed term. Users should visit the "Search Tips" link to the right of the Quick Search box for a list of stop or reserved search words. An example of a reserved word is ***and***. Typing ***and*** in a search box retrieves results including *and*rogen. Users who want to use AND as the Boolean operator should select the term from the drop-down menu in the search form. Users can type terms including numbers and letters in a search box in either Quick or Tab search boxes. Terms typed with punctuation such as an apostrophe, plus or minus signs, and curly brackets are placed in quotes by xPharm. For example, typing **N,N diethyl** results in the following xPharm treatment: **"N,N" AND diethyl**. Similarly, typing **Alzheimer's** results in the term treated as **"Alzheimer's."**

Users can search terms and then limit them to Agents, Targets, Disorders, or Principles, or search all four areas or a few of the areas at once. Extended functionality for this advance search includes four available search boxes, instead of the one found in Quick Search. Search operators include AND, OR, or NOT. It is therefore possible to engineer a much more complex search, building "hedges" of like terms if desired.

A search for **lupus or SLE** was performed and appears in Figures 6. The Disorder article, entitled "Systemic Lupus Erythematosus," was chosen. The article, written by Roselyn Cerutis, includes color hyper-

FIGURE 6. Main Search and Results for Lupus or SLE



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links like other xPharm summaries. Links referring to related Agents, Targets, and Disorders are appropriately identified (see Figure 7). Blue links, such as on the article author name, take users to external Web sites related to the topic. Other examples of blue links include authors referred to in the text of the article and their associated citations, journal citation information under "Bibliographic References," recommended Web sites such as <http://www.lupus.org>, and the site for the National Institute of Arthritis and Musculoskeletal and Skin Disorders (NIAMS) <http://www.niams.nih.gov/>.

INTERVIEW WITH RESEARCHER DEBBIE PERSAUD

The following contains information from an interview conducted by the author with researcher Debbie Persaud. It is presented in a question and answer style.

FIGURE 7. “Systematic Lupus Erythematosus” Article

discoverygate xPharm®

Home | Contents | Search | Agents | Targets | Disorders | Principles

Quick Search within All xPharm | Search Tips | About | Wizard

Systemic Lupus Erythematosus

Roselyn Ceruto

Click here to cite this article.

Introduction

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disorder. It is one of the most common autoimmune diseases, especially in women of childbearing age. The condition manifests with musculoskeletal, neuropsychiatric, renal, ocular, cardiovascular and pulmonary involvement. Because of the basic defects in immune cell function, there is underlying immune dysregulation that may predispose the individual to infection and might possibly increase the risk for cancer.

Definition

Systemic lupus erythematosus is a chronic, remitting and relapsing autoimmune disorder that is characterized by injury to many organs and to serosal membranes. The principal sites involved are the skin, kidney and joints. The intolerance to self results in the secretion of multiple autoantibodies that mediate vascular and organ damage.

Classification

Systemic lupus erythematosus is an autoimmune disorder. It belongs to the family of rheumatic diseases.

Consequences

There seem to be multiple abnormalities in the immune responses of those with systemic lupus erythematosus. The generation of tolerance is abnormal, as is activation, regulatory cell formation, apoptosis of self-reactive cells, idiotypic regulation and clearance of immune complexes.

Associated Disorders

Disorders associated with systemic lupus erythematosus include Discoid lupus erythematosus (DLE), thrombotic thrombocytopenic purpura Vasoo et al (2002), congestive heart failure, stroke, osteoporosis and non-Hodgkin's lymphoma Bongu et al (2002).

Etiology

The etiology of systemic lupus erythematosus is largely unknown. Genetics, environment, hormones and viruses may all contribute to the development of the condition Bongu et al (2002) Adelman and Marchalonis (2002) McMurray (2001). Some of the genes associated with systemic lupus erythematosus include human leukocyte antigen (HLA) HLA-DR3, HLA-DR2, Fcgamma receptors (FcgammaR) IIA and IIIA, and hereditary complement deficiencies. The loci have been identified on differing chromosomes for African-American and European-Americans see Moser et al (1998) Harley and Kelley (2002). Neuropsychiatric manifestations of the condition are linked to Systemic Lupus Erythematosus susceptibility 3 (SLEB3, = gene map locus 4p16-15.2) Nath et al (2002). Ultraviolet light, stress and viral infections can trigger flare-ups of systemic lupus erythematosus. Exacerbation of symptoms has been noted during normal menses and pregnancy. Chemicals, such as hydralazine, procainamide and D-penicillamine, can induce a systemic lupus erythematosus-like response in humans Portanova et al (1987). A chemical in alfalfa sprouts, L-canavanine, is also implicated Brown (2000).

Epidemiology

The prevalence of systemic lupus erythematosus in the United States and Europe is 15-68 per 100,000 persons. Women have an eight- to ten-fold greater risk of developing the condition than men. Indeed, after thyroid disease, it is the second most common immune disorder in women of childbearing age. While the disease may strike in younger or older people, females usually develop symptoms in a 12:1 ratio as compared to males during the childbearing years. Before menarche and after

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Pathophysiology

Antinuclear antibodies (ANA) are found in almost all those suffering from systemic lupus erythematosus. The ANAs are grouped into four categories, including those against DNA, those against histones, against non-histone proteins bound to RNA and against nucleolar antigens. The titer of serum ANAs is related to disease severity. As ANAs are not confined to systemic lupus erythematosus, the additional presence of autoantibodies to double stranded DNA (dsDNA) and Smith antigen virtually identifies the disorder. For a table of the antigens against which ANAs are directed see table 311-1: http://www.harrisonsonline.com/serverjava/Arknoid/amed/harrisons/co_chapters/ch311/_p05.html

The production of autoantibodies leads to immune complex formation. These immune complexes deposit in many tissues and contribute to the manifestations of this condition. The autoantibodies are also responsible for complement-mediated damage.

A large number of patients with systemic lupus erythematosus develop kidney problems due to immune complex deposition in the glomeruli. In addition, the complexes can be deposited in the lungs, mesothelium, synovium, skin and other sites.

Biopsies of facial rash show immune complex deposition. Renal biopsies are often used to determine the degree of immune complex deposition and to decide on therapeutic interventions. IgG3 antinucleosome antibodies are a significant subgroup of ANA present in active lupus nephritis. Other anti-self antibodies present are anti-Ro (SS-A) and anti-La (SS-B).

In the joints, immune complex deposition often leads to arthralgia. If the mesothelium is involved, effusions can form in body cavities.

The lungs may be affected in systemic lupus erythematosus, with pleuritis and pleural effusions occurring in almost 50% of patients. More rarely, there can be edema and hemorrhage because of alveolar injury or chronic interstitial fibrosis.

Many patients with systemic lupus erythematosus also have antiphospholipid syndrome (APS), characterized by antibodies directed towards proteins complexed to phospholipids (aPLs), venous and arterial thrombosis, repeated fetal loss or thrombocytopenia. The syndrome can be either primary or secondary to a systemic condition. These patients have a higher prevalence of endocarditis with valvular involvement (Libman-Sacks endocarditis) than those without these antibodies. Valve masses (nonbacterial vegetations) occur. The mitral valve is more prone to involvement than the aortic valve, regurgitation being the predominant functional abnormality Hojnik et al (1996).

The presence of antineuronal IgG is associated with diffuse central nervous system lupus. Antiribosomal P antibody may be linked to depression or psychosis. In pediatric-onset systemic lupus erythematosus, serious central nervous system symptoms, such as seizures, major cognitive disorder, chorea, psychosis, major depression and acute confusional state, are more common than glomerulonephritis Sibbitt et al (2002).

Central nervous system involvement is believed to be caused by ischemia precipitated by coagulation abnormalities, vessel wall thickening, focal atherosclerotic plaques in larger arteries and inflammatory processes in some cases. These manifestations and a review of the central nervous system symptoms associated with systemic lupus

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Interviewer: *How did you like xPharm?*

Persaud: It saved hours of time in looking for primary research articles that are specific to my research model (e.g., rat, dog, human, or cell line). Information is well organized and easily accessible. For instance, I was interested in Coagulation Factor IX as a target for the development of potential antithrombotic drugs. All I had to do was type in *Factor IX* in xPharm's search box and all of the information I desired, including physiological function in humans, probes that have already been characterized, pharmacological activators and antagonists, were cited in over 100 journal articles. Prior to using xPharm, I tried a search on Ovid MEDLINE. I had combined the search queries *Factor IX* and Drug Delivery Systems, resulting in only seven articles.

Interviewer: *Can you summarize key benefits and/or drawbacks to xPharm?*

Persaud: Benefits include the following:

- Direct links to primary literature.
- Links to Material Safety Data Sheets (MSDS). (You need to know this basic information before starting to use a compound in the lab. You'd have to read through regular literature to find this or wait to obtain the information after you purchased the drug from a distributor. But often, I want to see the MSDS way before I purchase a compound. I may not even want to use the compound after I see the MSDS.) [In response to the Interviewer's question about whether MSDS sheets could be located on the Internet, Ms. Persaud clarified that MSDS sheets for some compounds are not that easy to locate. Also, a compound being sold by a distributor can be sold under a variety of synonyms, making it difficult to locate the MSDS in advance.]
- Distinction between using a drug as an *Agent* versus *Target*. This is something researchers have to distinguish on their own when reading through journal articles.
- Inclusion of pre-clinical research to assess MTD (Maximum Tolerated Dose) in animal models early in the research discovery process. You can use the MTD to gauge parameters for your own assay.

- Experts in the field summarize complex drug interactions between compounds in multiple biological models and disease states.
- Teaching aids such as the figure and accompanying annotation, "Overview of Hemostasis," cited in the Principle entry "Coagulation Factors" are thorough and easy to understand (see Figure 8).

Drawbacks to xPharm, as stated by Ms. Persaud, are as follows:

- I wish there was another tab entitled chemical patents incorporated in this product. Although a separate product called "MDL Patent Chemistry Database" is offered. (An xPharm representative notes that many companies subscribe to MDL Patent Chemistry Database, which then can be added with xPharm via the DiscoveryGate platform.)
- I wish some of the teaching aids were animated.

Interviewer: *Is there a similar drug resource that you have used in your present or past research work?*

Persaud: As I mentioned previously, I have used MEDLINE, but it is no comparison. xPharm brings all the information I need together in one place. There are even hyperlinks to the genes associated with a target, including some genes not listed in MEDLINE.

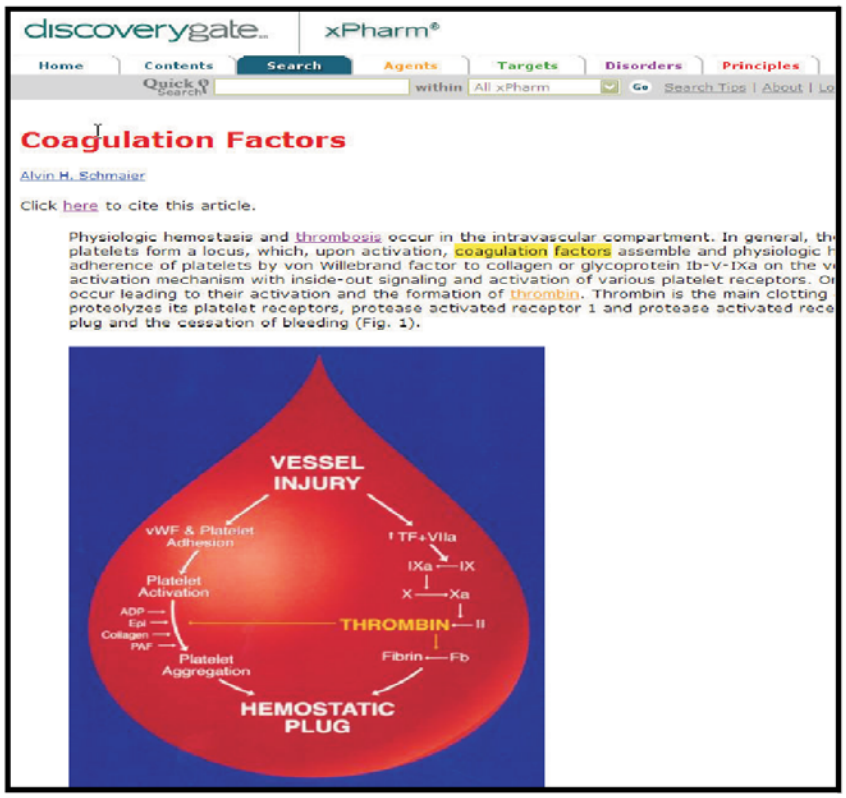
Interviewer: *Do you feel that xPharm appeals to a certain group of researchers-undergraduates, graduate students, drug company new hires, seasoned researchers?*

Persaud: All of the above groups could benefit from its use–they are all looking for a place to get the most comprehensive and up-to-date information for a certain topic.

KEY POINTS TO REMEMBER

xPharm is not a database meant to aid clinical pharmacy or medical practitioners. Pharmacologic or experimental drug doses that are contained in xPharm articles are not treatment doses. A product such as Micromedex may prove more suitable for reviewing drug doses for pa-

FIGURE 8. Overview of Hemostasis



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tients encountered in clinical practice. Further, xPharm does not focus solely on agents or compounds, but the relationship of agents to biological targets and other relationships in that mix. For example, users can review all the agents that interact with D_2 dopamine receptors, excluding thiazides.

Relational queries possible in xPharm cannot be executed in PubMed at this time. xPharm is an appealing product for many researchers involved in drug discovery. Biologists will look at which agents act on which targets. Medicinal chemists and pharmacologists will value the section on agent-agent interaction.

FOR THE FUTURE

The Disorders article, "Pain," by Frank J. Dowd notes version two under his name. With each progressive article update, section highlights noting changes or additions may prove useful. A record of deletions from a summary may also be warranted.

Breadcrumb navigation or a drop-down box showing where users have searched or what pages users have visited, is another idea of a useful addition to xPharm; users may forget pages that they have already reviewed. For instance, after clicking "M" in the A-Z contributor list, a Principles article by Paul Moser and Michael Williams was discovered, entitled "Use of Animal Models for Drug Discovery." Also, getting back to the original search before the digression proved time consuming.

At the time of this review, xPharm was in version 1.0 release. As mentioned previously, the product is updated quarterly. Users should expect the following from the September 2005 update.

- xPharm records on infectious diseases including Influenza A, and Hemophilus Infections
- xPharm principle records (part of a series) on Safety Pharmacology Look for "Safety Pharmacology–CV, GI, Respiratory and Renal Safety" and "Safety Pharmacology–Target Binding Profile" articles.
- Update of 14 adrenoreceptors, addition of a cluster of new chemokine receptors, and a record on "CRF-1 Corticotrophin Releasing Factor Receptor."

CONCLUSION

Much of medical and academic librarianship focuses on supporting clinical researchers. Many databases listed on library Web pages do not reflect the initial stages of health science research, let alone the specific area of drug discovery. The medical library of the future may consider the above when making subscription purchases and in collection development decisions. Identifying products and hosting trials of drug discovery products may prove valuable to campus researchers, regardless of whether the library can afford the products trialed. xPharm is an example of a product that can be shown to research patrons involved in drug discovery research at institutions of higher learning.

FOR MORE INFORMATION

Elsevier MDL
14600 Catalina Street
San Leandro, CA 94577
510.895.1313 (Phone)
510.895.5502 (Fax)

For Trialing and Pricing:
800.955.0051 (Your Elsevier Account Manager)
E-mail: nasales@mdl.com
<http://www.mdl.com/products/knowledge/xpharm> (on xPharm)

xPharm offers a 14-day individual trial or a 30-day trial for institutions.

APPENDIX

Drug Research & Development Intelligence Kit

DATABASES

R & D Insight *(ADIS International)*
<http://bi.adisinsight.com>

R & D Insight follows a drug through its life cycle from discovery to discontinuation or launch and beyond. Drug or compound tracking dates back to 1986. ADIS ratings mark the therapeutic value of a compound. Compound summaries, including chemical structure images can be exported to create custom alerts via BizInt Webcharts software.

IDdb3–The Investigational Drugs Database *(Thomson Current Drugs)*
<http://www.iddb3.com>

This competitive intelligence drug database covers the pharmaceutical and biotechnology industry. The database, updated daily, provides alerts on drugs, from their patent to launch to post-marketing phase. Alerts on drug companies and meetings are also accessible. The product can be used to create alerts on a

drug or drug class. These personal alerts can be exported to Microsoft Excel or a Webchart tool such as BizInt.

Pharmaprojects *(PJB Publications Ltd)*
<http://www.pjbpubs.com/pharmaprojects/index.htm>

This research and development (R & D) product is a subscription product that includes a version available for the Web. The database boasts 25 years of global R & D vigilance. Pharmaceutical, biotechnology and chemistry-geared companies can benefit from Pharmaprojects. This product will allow a user to identify partners for drug research and marketing, monitor competitor drug pipelines, and even link to Internet gene databases.

Prous Integrity *(Prous Science)*
<http://integrity.prous.com/integrity>

This is a research and development portal useful to scientists such as biologists, medicinal chemists, and pharmacologists working in all phases of drug discovery. From this portal access Prous Daily Drug News highlights, conference and congress updates, as well as information on drug targets, pipelines, and clinical trials. Various search engines are available for finding information in "Knowledge Areas." Areas include "Drugs & Biologics," "Pharmacokinetics/Metabolism," "Disease Briefings," and "Companies & Markets."

NEWS SOURCES

Prous Science Daily Drug News *(Prous Science)*
<http://www.dailydrugnews.com/home_daily>
<http://www.dailydrugpatents.com>

Subcribe to the Prous Science products above and receive daily e-mail headlines on pharmaceutical drug and patent news respectively. Prous Daily Drug News possesses a clean interface. Daily Drug News producers monitor the Internet, regulatory agencies, patents, and congresses, to name a few, in order to bring users the most relevant and up-to-date information, including chemical structures when available. Users who like Daily Drug News may consider subscribing to Prous Science Daily Patent News. The Patent News Web site has a demo worth reviewing for features of this unique product.

APPENDIX (continued)

First Word *(P\S\L Group)*
<http://main.pslgroup.com>

Sign up for free daily Auto-Alerts via e-mail of this business intelligence resource. This site offers brief industry and medical information on the latest drug pipeline developments and/or regimens for specific condition, as well as pharmaceutical industry news such as mergers and company losses.

Biospace *(Biospace)*
<http://www.biospace.com/index.cfm>

Biospace, like First Word, allows you to subscribe to a free daily e-mail alert. Key site features include the Biospace portal with links to news feeds for researchers in the life sciences, as well as researchers in other health related fields. Pharmaceutical industry and drug news are also included in this gem, making it a "must have" for any researcher looking for competitive intelligence information on the Web.