Relevance of Chemistry In Drug Discovery

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Drug Design & Discovery

Drugs: Natural sources

Targets: Synthetic sources
What is a drug?

A Chemical Substance that Interacts with a Living System and Produces a Biological Response
What is a drug?
Over 100 Different Disciplines Working Together
Drug Discovery & Development

Identify disease

Isolate protein involved in disease (2-5 years)

Find a drug effective against disease protein (2-5 years)

Preclinical testing (1-3 years)

Scale-up

File IND

Human clinical trials (2-10 years)

File NDA

Formulation

FDA approval (2-3 years)

Drug Design

- Molecular Modeling
- Virtual Screening
Technology is impacting this process

Identify disease

Isolate protein

COMBINATORIAL CHEMISTRY
Rapidly producing vast numbers of compounds

MOLECULAR MODELING
Computer graphics & models help improve activity

GENOMICS, PROTEOMICS & BIOPHARM.
Potentially producing many more targets and “personalized” targets

HIGH THROUGHPUT SCREENING
Screening up to 100,000 compounds a day for activity against a target protein

VIRTUAL SCREENING
Using a computer to predict activity

Find drug

IN VITRO & IN SILICO ADME MODELS
Tissue and computer models begin to replace animal testing

Preclinical testing
DRUG DISCOVERY PROCESS

Target Identification and Validation

High-Throughput Screening

Chemical Libraries, CombiChem, Natural Products

Lead Compounds
Evaluation
Clinical Trials
Who discovers drugs? Doctors?

- Identify biological target - biology
- Prioritise/validate target – pharmacology and chemistry
- Identify and optimise lead molecules – chemistry/pharmacology
- Preclinical studies – chemistry/pharmacology/toxicology
- Formulation - pharmaceutical sciences
- Clinical evaluation – medicine
- Manufacture - chemical engineering
Chemistry is the study of matter, its properties, how and why substances combine or separate to form other substances, and how substances interact with energy. Many people think of chemists as being white-coated scientists mixing strange liquids in a laboratory, but the truth is we are all chemists.
MEDICINAL CHEMISTRY

- It is a stimulating field as it links many scientific disciplines and allows for collaboration with other scientists in researching and developing new drugs.
- Medicinal chemists apply their chemistry training to the process of synthesizing new pharmaceuticals.
- Medicinal chemists are focused on drug discovery and development and are concerned with the isolation of medicinal agents found in plants, as well as the creation of new synthetic drug compounds.
Most chemists work with a team of scientists from different disciplines, including biologists, toxicologists, pharmacologists, theoretical chemists, microbiologists, and biopharmacists. Together, this team uses sophisticated analytical techniques to synthesize and test new drug products and to develop the most cost-effective and environmentally friendly means of production.
The role of organic chemistry in pharmacy

- Organic chemistry is the base of pharmacy, without chemistry a pharmacist cannot understand the chemical formulae of the drugs and the design of new drugs.
- A pharmacist cannot practice in the field of pharmacy without a good knowledge of chemistry.
Additionally, organic chemistry deals with life and life processes, being associated with nearly every aspect of our existence.

All the key molecules of life, such as DNA, proteins, lipids and carbohydrates, are organic compounds, furnishing the energy that sustains life.
Analytical Chemistry in Drug Discovery/Pharmaceuticals

• Analytical chemistry is the branch of science that provides knowledge of compound separation, identification and quantification that can be useful for measuring bioavailability of drugs, purifying drugs during synthesis, and identifying drug metabolic pathways.

• To accurately quantify drugs and metabolites in pharmacokinetic, transport, and delivery studies, a strong understanding of analytical chemistry principles is necessary and only well-characterized analytical methods should be used to ensure the integrity of collected data.
• The foundation of the pharmaceutical industry includes a group of highly skilled chemists.
• The manufacturing of bulk drugs or commercial drugs involves the direct supervision of chemists, who are involved in the R&D process of pharmaceuticals where new drugs are designed and synthesized.
• The manufacturing of dosage forms like tablets, capsules and injections has to be done under the strict supervision of qualified pharmacists.
The Drug Discovery Process

Target selection & validation
- Animal Studies
  - relevant species
  - transgenic KO/KI mice
  - conditional KOs
  - agonists/antagonists
    - antibodies
    - antisense
    - RNAi
- Molecular Studies
- Studies of Disease Mechanisms

Discovery
- Target
  - receptor
  - ion channel
  - transporter
  - enzyme
  - signalling molecule
- Lead Search
  - Develop assays (use of automation)
  - Chemical diversity
  - Highly iterative process
- Lead optimization
  - selectivity
  - efficacy in animal models
  - tolerability: AEs mechanism-based or structure-based?
  - pharmacokinetics
  - highly iterative process

Development
- Drug Candidate safety testing
- Human Studies Phases I, II, III
- Drug Approval and Registration

The Drug Discovery Process
Target Selection & Validation

- Define the unmet medical need (disease).
- Understand the molecular mechanism of the disease.
- Identify a therapeutic target in that pathway (e.g. gene, key enzyme, receptor, ion-channel, nuclear receptor)
- Demonstrate that target is relevant to disease mechanism using genetics, animal models, lead compounds, antibodies, etc.
Discovery

- Develop an assay to evaluate activity of compounds on the target
  - *in vitro* (e.g. enzyme assay)
  - *in vivo* (animal model or pharmacodynamic assay)

- Identify a lead compound
  - screen collection of compounds (“compound library”)
  - compound from published literature
  - screen Natural Products
  - structure-based design (“rational drug design”)

- Optimize to give a “proof-of-concept” molecule—one that shows efficacy in an animal disease model

- Optimize to give drug-like properties—pharmacokinetics, metabolism, off-target activities

- Safety assessment, Preclinical Candidate!!!
Clinical Trials

Phase I
20 - 100 healthy volunteers take drug for about one month

Phase II
Several hundred health-impaired patients
Treatment Group  Control Group

Phase III
Hundreds or thousands of health-impaired patients

Investigational New Drug application
IND

Product Profile  Marketing SOI

Information Learned
1. Absorption and metabolism
2. Effects on organs and tissue
3. Side effects as dosage is increased

Information Learned
1. Effectiveness in treating disease
2. Short-term side effects in health-impaired patients
3. Dose range

Information Learned
1. Benefit/risk relationship of drug
2. Less common and longer term side effects
3. Labeling information

Compassionate Use
**Clinical Trials Continued**

- **Submit to Regulatory Agencies**
- **Advisory Committee**
- **Regulatory Review Team**
  - Reviews, comments, and discussions
  - Drug Co./Regulatory liaison activities

**New Drug Application (NDA)**

**APPROVAL PROCESS (Ex. FDA)**

**APPROVAL**

Worldwide Marketing Authorization (WMA) in other countries
Drug Discovery—Convergence of Disciplines

- Combinatorial Chemistry
- Synthetic Chemistry
- Patent Law
- Intellectual Property
- Physiology
- Biochemistry
- Pharmacology
- Immunology
- Enzymology
- Physical Chemistry
- Pharmacokinetic Properties
- DMPK

- Design
- Novel Molecule
- Modelling
- Information Technology
- Safety Assessment
- Safety
- Metabolism
- Pharmacology
- Pathology
- In Vivo activity
- Behaviour
- Physiology

- Medicine
- Pathology
- Pharmacology
- DMPK
Green Chemistry as a Recent Trend in Pharmacy Education to Afford Pharmaceutical Products

“Chemistry has an important role to play in achieving a sustainable civilization on earth.”
Twelve principles of green chemistry

1. Prevention.
2. Atom Economy.
3. Less Hazardous Chemical Synthesis.
4. Designing Safer Chemical.
5. Safer Solvents and Auxiliaries.
7. Use of Renewable Feedstock.
8. Reduce derivatives.
10. Design for degradation.
12. Inherently safer chemistry for Accident Prevention.
I've always been confident. Especially having confidence that one day I'd be very successful or do things right.

But in 2011, I noticed something that was stopping me.

What was it?

Simply put I talked more than I acted.

I consumed more than I acted.

And I said I wanted certain things in life, but my actions were quite different.

I objectively noticed that what I was saying and what I was doing were very far apart.
And that's a common challenge I see with people who aren't getting the results they want in life.

You want to have success, you want to get rich, but you may not be taking the consistent actions to get there.

Successful people are willing to do what unsuccessful people won't do. Look at your life right now. Can you confidently say you're doing that?
Or are you talking about it more than acting on it, like I did?

The reason I bring this up is because it's crucial to notice.
Good or good?

Look at your actions vs. what you are saying.

Are they supporting each other?
QUESTION ?
Thank You

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