SAMPLE PREVIEW

BPS3012

Applied Pharmaceutical Science

From Concept to Market

Comprehensive Study Notes

HD 84 • Monash University

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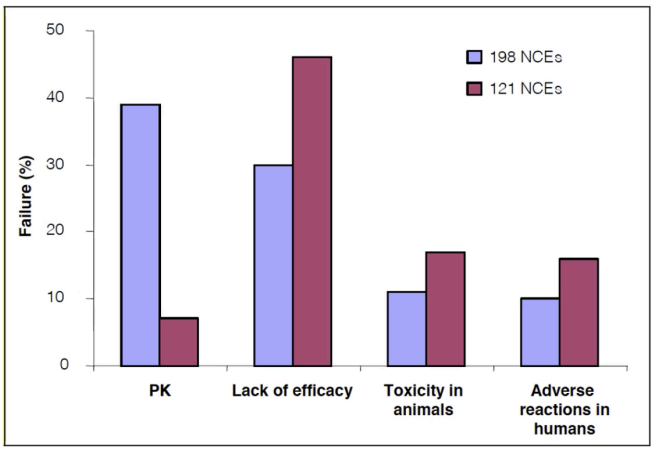
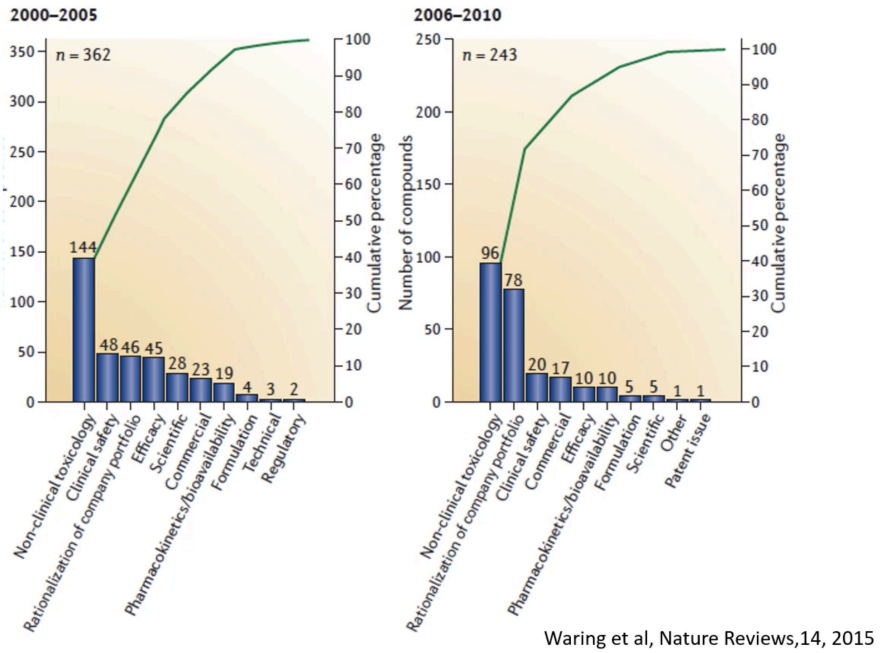
BPS3012 Applied Pharmaceutical Science: From Concept to Market

Factors contributing to drug failures

- Pharmacokinetic properties
- Lack of efficacy
- Toxicity in preclinical studies
- Adverse reactions in clinical studies
- Formulation challenges
- Commercial decisions
- Portfolio rationalization



NCE = new chemical entity
Blue = 1960s, red = 1980s



Waring et al, Nature Reviews,14, 2015

Learning outcomes

Describe the key reasons why drugs fail during development.

- Insufficient therapeutic effect in the target population
- Inadequate efficacy demonstrated in preclinical or clinical studies
- Unacceptable side effects or toxicity.
- Poor trial design or endpoints
- Failure to meet regulatory requirements
- Limited market potential or competitive landscape
- High development costs
- Lack of physician or patient acceptance
- Inadequate animal models or predictive tests
- Limited understanding of the drug's mechanism.

Describe how the approaches taken to drug discovery and development have influenced the reasons for drug failure over time

Traditional Approaches (Early to Mid-20th Century)

- Relied on trial and error due to a limited understanding of diseases and drug mechanisms
- Used large compound libraries without precise target knowledge
- Lack of target specificity led to high attrition rates
- Chance findings led to successes but also unexplained failures (serendipity)

Molecular Biology and Rational Design (Late 20th Century - Early 2000s)

- Advances in molecular biology enabled the identification of specific disease targets
- Structure-based approaches aimed at designing compounds to fit target structures
- Improved target understanding and reduced failures due to lack of efficacy
- A better understanding of target interactions helped predict adverse effects
- Limited success in some complex diseases, and off-target effects remained concerns

Genomics and High-Throughput Screening (2000s - Early 2010s)

- Genomic information enabled the identification of disease-related genes
- Automated assays tested large compound libraries against specific targets
- Enhanced understanding of genetic basis improved target selection
- Limited translation from preclinical to clinical success
- Some target pathways had unforeseen systemic effects

Personalized Medicine and Precision Approaches (2010s - Present)

- Individualized patient characteristics guide target selection
- Drugs designed for specific genetic or molecular subsets
- Improved outcomes due to patient-specific treatment
- Limited patient populations may restrict commercial viability
- Flexible trial designs accommodate changing patient data

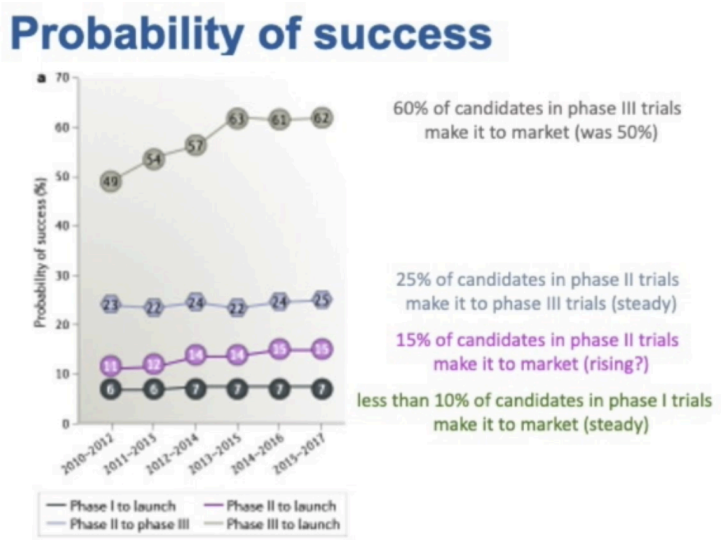
Data-Driven and AI-Assisted Approaches (Present and Future)

- Utilizing large datasets to identify novel targets and predict outcomes
- Algorithms predict drug-target interactions and potential side effects
- Faster identification of potential leads and better target validation
- The reliability of AI predictions remains a challenge
- Balancing data use and patient privacy

<u>Evaluate the consequences of drug failure in the broader context of drug discovery and development.</u>

- Financial impact = High Cost = Development costs, including research, clinical trials, and manufacturing, are substantial
- Failed drugs result in significant financial losses
- Funds that could have been used for other projects are diverted (opportunity cost)
- Drug discovery and development is time-consuming (opportunity cost)
- Resources spent on failed projects could have been utilized for more promising candidates
- High failure rates may discourage innovative and risky projects
- Failed drugs may leave patients with limited treatment options for certain conditions.
- Repeated failures may erode public trust in pharmaceutical industry claims
- Failed drugs may result in missed opportunities to capture market share
- Companies must compete against other firms to secure a foothold in the market

Why Drugs Fail blog summary

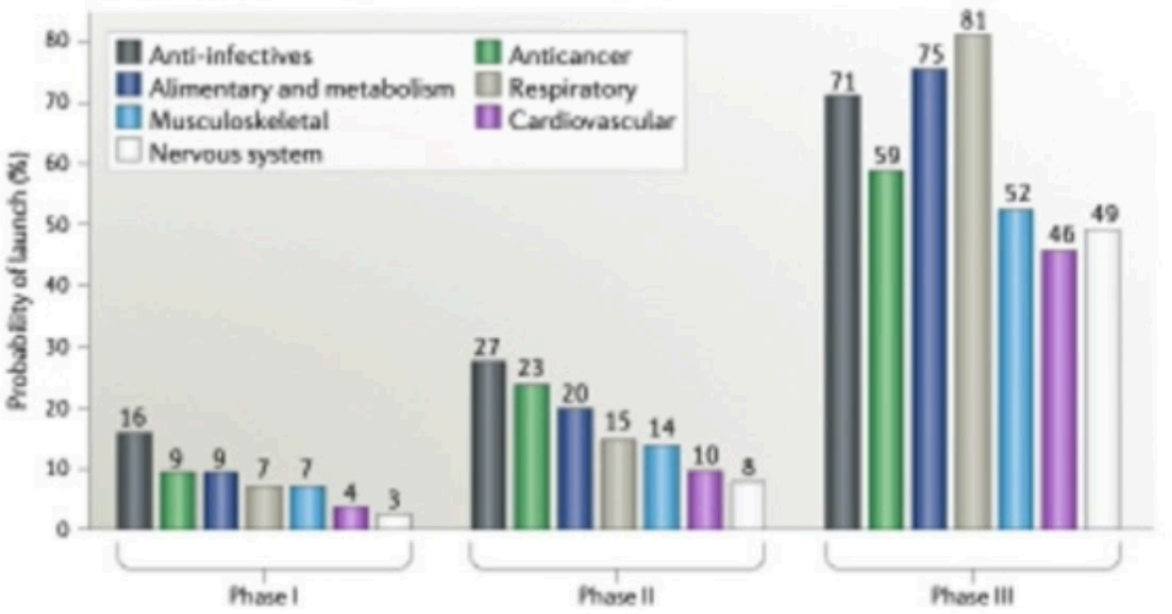


- <u>Statistics:</u>
  - <10% of candidates in phase I trials make it to market
  - 15% of candidates in phase II trials make it to market
  - 25% of candidates in phase II trials make it to phase III trials
  - 60% of candidates in phase III trials make it to market

- FDA approvals increased to 59 in the past year, raising questions about whether this trend is significant or random

- Compound success entering Phase I trials remains around 10%
- Success rates in Phase III trials have increased in recent cohorts
- Phase II to Phase III success rates have remained consistent
- Failures are primarily due to efficacy and safety issues, revealing gaps in understanding
- Therapeutic areas like CNS and cardiovascular drugs have lower success rates in Phase III

Different diseases and failure rates



- Higher failure rate and lower probability of launch for cardiovascular and nervous systems
    - Complexity of disease mechanism
    - Lack of suitable biomarkers
    - BBB penetration challenges
    - Regulatory hurdles
    - Patient variability
    - Limited animal models

Failed drugs

- The drug candidates that organizations
    - Companies
    - Academic institutions
      Reasonably expected will be suitable as drugs
      (candidate drugs in the timeline diagram/pipeline)
- Not hits and leads
    - Part of the process, not necessarily failures

Failures and the cost of drug discovery and development

- Average cost $1-3 billion, 10+ years
- Complex, difficult to determine precisely
    - Obtaining data from companies

PREVIEW

Get the full notes

A free preview of the complete BPS3012 notes.
The full set is 43 pages, covering every topic with all diagrams and a clickable table of contents.

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