

Definitions

Synthetic Drug A drug of human origin. Made in a laboratory rather than being extracted from a plant or other ecological source

Medicinal Chemistry Branch of chemistry that is concerned with design, development and synthesis of pharmaceutical agents or medicines. Medicinal chemists find the relationship between the structure of a drug and its pharmacological or toxicological properties

Animal Model A living, non-human species that is affected by a specific disease. Which is usually of relevance of human pathology. These animal models are used during the testing of new and unproven treatments for the diseases without initially involving actual humans suffering from the disease

Pathogen An infectious agent that causes disease or illness in a host.

Definitions (cont)

Pathogenesis The development of a disease and the chain of cellular and tissue events leading to the manifestation of the disease in people.

Human Safety Concerns

A drug that is safe for animal isn't always safe for humans

Only 70% of drugs that are toxic on animals are toxic in humans

Some animal organ model are inaccurate (i.e skin brain and liver models)

Some toxic effects are hard to detect in animal models (hearing loss)

Each animal has a different metabolising speed

Classic Animal Models

Zucker Diabetic Rat and SHR Rat assisted in the search of drugs for cardiovascular and metabolic diseases

German Pharmaceutical Industry / Coal

The widespread use of coal led to a vast quantity of coal tar. coal tar is rich with small organic molecules which can be used to build more complex ones. Germany dominated in creating synthetic drugs for several reasons

A) Establishment of in house research labs

B) Creation of partnerships between researchers and academic

C) Creation of partnerships between university departments and research students

Examples of Animal Models

Chloral Hydrate (1869) By: Oscar Liebreich
Use: Sleep Inducing
Tested: Rabbits

Barbitone (1903) By: Emily Fischer
Use: Hypnotic Effect
Tested: Dogs

Prontosil (1935) By: Gerhard Domagk
Use: Streptococcus
Tested: Mice

Phenytoin (1936) By: Tracey Putnam
Use: Anticonvulsant
Tested: Cats

Diphenhydramine (1943) By: Daniel Bovet
Use: Antihistamine
Tested: Guinea Pigs

Librium (1957) By: Leo Sternbach
Use: Tranquilliser
Tested: Mice, Cats, Dogs, Monkeys

Ibuprofen (1969) By: Stewart Adams
Use: Anti-inflammatory
Tested: Rabbits

Omeprazole (1979) By: Astra
Use: Heartburn
Tested: Rats, Dogs

Disease Relevance Issues

Animal Models can never be truly precise and indicative of human disease

Drugs that work on Animal Models don't always work on Humans

Some diseases are too complex to reproduce in animals



Paul Ehrlich

Father of Chemotherapy

Born in Silesia

Worked with synthetic dyes

Noted that some dyes entered certain tissues but not others

Led to the theory that chemicals can be designed to selectively enter certain tissues

"magic bullet theory"

Stages of Syphilis

Infection Bacteria T.Pallidum enters host

First Firm and painless skin lesions at stage site of infection.

Second Skin rash, Swollen lymph nodes, Stage Sore throat, Patchy hair loss, headaches, Weight loss, Muscle aches

Latent Symptoms may subside for months or years

Final Deterioration of cardiovascular Stage system. May result in dementia or blindness

Ethical Concerns

Refinement Minimise suffering to individual animal's experience

Reduction Only use as many animals as needed
Reduce number of tests
test multiple things at once

Replacement Find alternate testing Methods

Disease Model Testing

Compound A large set of structurally Libraries similar molecules
by testing each one we can identify related molecules with similar properties

Animal A safe way to identify Models promising drugs
used to screen compound libraries

Trained Impartial unbiased scientifi- Invest- cally trained observers
igators

Disease A measurable indicator of a Biomarkers disease
used for diagnostic purposes

There is no 100% safe way to test a drug

Compound 606

Dr Hata tested a compound library on rabbits. The 606th compound was effective. Named arsphenamine or salvarsan
It was hard to dissolve in water and was unstable. It had to be prepared onsite and injection was painful. 25-30 injections were needed.

