Drug Chemistry and Technology Basics,
Cleaner Production and Mega-Trends in Pharmaceutical Industry

Falsification of Medicines

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Questions

1. Why the discovery of a new drug is a long and costly process? Explain the different stages involved
2. What is QSAR?
3. What new sciences and technologies as drivers for drug discovery innovation do you know?
4. How chemistry connects with biology in drug design?
5. What risks exists in new drug development?

Questions

6. What quality standards in the field of medicines do you know?
7. What agencies for the evaluation of medicinal products do you know?
8. What is GLP, GCP, GMP, GSP, GDP and GPP?
9. What is preclinical research?
10. What phases of clinical research do you know?
11. The API of a specific stereoisomer is costly compared with the racemate. Can you find any reason for this? Justify why in some cases racemic APIs cannot be used as a medicine

LECTURES

1. Introduction
2. Terminology of Drugs
3. Drug Design and Quality standards
4. → Falsification of Medicines
5. Quality Assurance in Medicines
6. Control by Pharmacopeias
7. Trends in Pharmaceutical Industry

Falsified Medicines

Until recently, the most frequently falsified medicines in wealthy countries were **expensive "lifestyle" medicines**, such as hormones, steroids and antihistamines. In developing countries, they have included medicines used **to treat life-threatening conditions** such as malaria, tuberculosis and HIV / AIDS

The phenomenon of falsified medicines is on **the increase, with more and more medicines now being falsified**. These include expensive medicines, such as anticancer medicines, and medicines in high demand, such as antivirals

Types of Medicinal Product Affected by Counterfeiting

- ✓ high volume (high level of prescribing)
- ✓ high price
- ✓ known brand
- ✓ “lifestyle”/non-reimbursed
- ✓ blockbusters
- ✓ parenterals (in developing world)
- ✓ all generics
- ✓ off-label use drugs

(he use of pharmaceutical drugs for an unapproved indication or in an unapproved age group, dosage, or route of administration)

Medicinal Product

***Medicinal product** – a dosage form of medicine used for prophylaxis, diagnostics, treatment of disease, rehabilitation, as well as for maintenance, prevention or interruption of pregnancy

4 features of medicinal products (WHO):

1. **presence of a active pharmaceutical ingredients (API)**
2. **use for the treatment, prophylaxis, diagnostics**
3. **state registration as a drug**
4. **licensed industrial production**

Products received the pharmaceutical market

Compliance with **all four features** of medicinal products

Compliance with **the right of industrial property**

Compliance with **quality standards**

Product

Full ⇓ **drug**

Incomplete ⇓ **not a drug**

Original ⇓ **original drug**

Legal copy ⇓ **generic**

Illegal copy ⇓ **counterfeit drug**

Fake ⇓ **fake**

Full ⇓ **certified drug**

Incomplete ⇓ **defective (substandard) drug**

fake (falsified) drug

Terminology

The multiplicity of definitions and terminology – sometimes varying from one country to another – contributes to the lack of clarity around the problem and its global understanding

European citizens mainly use the term "**counterfeiting**", or more recently the term "**falsification**"

While **Americans** more readily use the terms "**false**" or "**fake**"

Falsified vs. Counterfeit Medicines

Falsified medicines are **fake medicines** that are designed to **mimic real medicines**

Counterfeit medicines are medicines that **do not comply with intellectual-property rights** or that infringe trademark law

The **WHO** defines **counterfeit medicine** as one which is deliberately and fraudulently mislabeled with respect to identity and/or source

Counterfeiting can apply to both branded and generic products and counterfeit products may include products with the correct ingredients or with the wrong ingredients, without active ingredients, with insufficient active ingredients or with fake packaging

Substandard medicines

Substandard medicines are pharmaceutical products that do not meet quality standards and specifications

Substandard drugs (also called '**out of specification products**') are genuine medicines produced by manufacturers authorized by the National medicines regulatory authority which do not meet quality specifications set for them by national standards

Only a small proportion of substandard drugs are falsified; the rest reach the market as a result of poor manufacturing practices, inadequate quality-control processes, incorrect storage or inappropriate packaging, or a combination of these factors

Counterfeit Medicines

Types of Counterfeit Medicines

- ✓ Correct drug, correct ingredients
- ✓ Wrong ingredients, but therapeutically active
- ✓ Wrong quantity of ingredients
- ✓ No active ingredients
- ✓ Toxic ingredients:

1990 Nigeria – 109 children die after taking a fake preparation containing diethylene glycol

1992 Bangladesh – paracetamol preparation containing diethylene glycol believed to have killed hundreds of children

1995 Haiti – 30 children die after taking medicines containing diethylene glycol

1998 India – 30 infant deaths (diethylene glycol)

2006 China – 11 people died from an antibiotic which was not properly sterilized

Types of Counterfeit Medicines

- ✓ …
- ✓ False labeling in respect of:
  - the authenticity of the drug
  - source (origin) of drug
- ✓ Forgery packaging

Falsified Drugs

So falsified drug as any drug with **a false presentation** of at least one of the following characteristics:

- ✓ Its **identity**, including its **packaging** and **labelling**, its **name** or its **composition** with regards to any of the ingredients, including excipients, and the strength of those ingredients
- ✓ Its **source**, including its **manufacturer**, its **country of manufacture**, its **country of origin** or of its **marketing authorization**
- ✓ Its **history**, including **records** and **documents** relating to the distribution channels used *(This definition does not include unintentional quality defects and is without prejudice to intellectual property rights violations")*

Manufacturers' Secure Packaging

- ✓ Tamper-proof outer packaging
- ✓ Covert markers *e.g. Cryptoglyph* encryption
- ✓ Radiofrequency identification (RFID)
- ✓ Holograms
- ✓ Security Inks
- ✓ 2-D Bar Coding
- ✓ Medicines Passports (Pedigrees)

*Research is under way to use **nuclear quadruple resonance spectroscopy** to detect counterfeit or substandard drugs without removing the product from its packaging. Nuclear quadruple resonance can analyze compounds containing C, Cl, Br, Na, and K atoms, which constitute over 80% of all drugs*

Manufacturers' Secure Packaging

In July 2011, the **EU** strengthened the protection of patients and consumers by adopting a new **Directive on falsified medicines for human use**

The Directive came into force on 21 July 2011. Member States had to start applying its measures in January 2013

On 9 February 2016, the European Commission published a delegated regulation (**Commission Delegated Regulation (EU) 2016/161**) that introduces two safety features to be placed on the packaging of most human medicines:

- ✓ a **unique identifier** (a 2-dimension barcode) and
- ✓ **anti-tampering device**

Security

- ✓ serially control of each batch of drugs entering the country
- ✓ acceptance quality control of drugs in pharmacies and the wholesale sector
- ✓ interaction of control and analytical laboratories with foreign drug production companies
- ✓ information from analytical laboratories about rejected and falsification of drugs facts

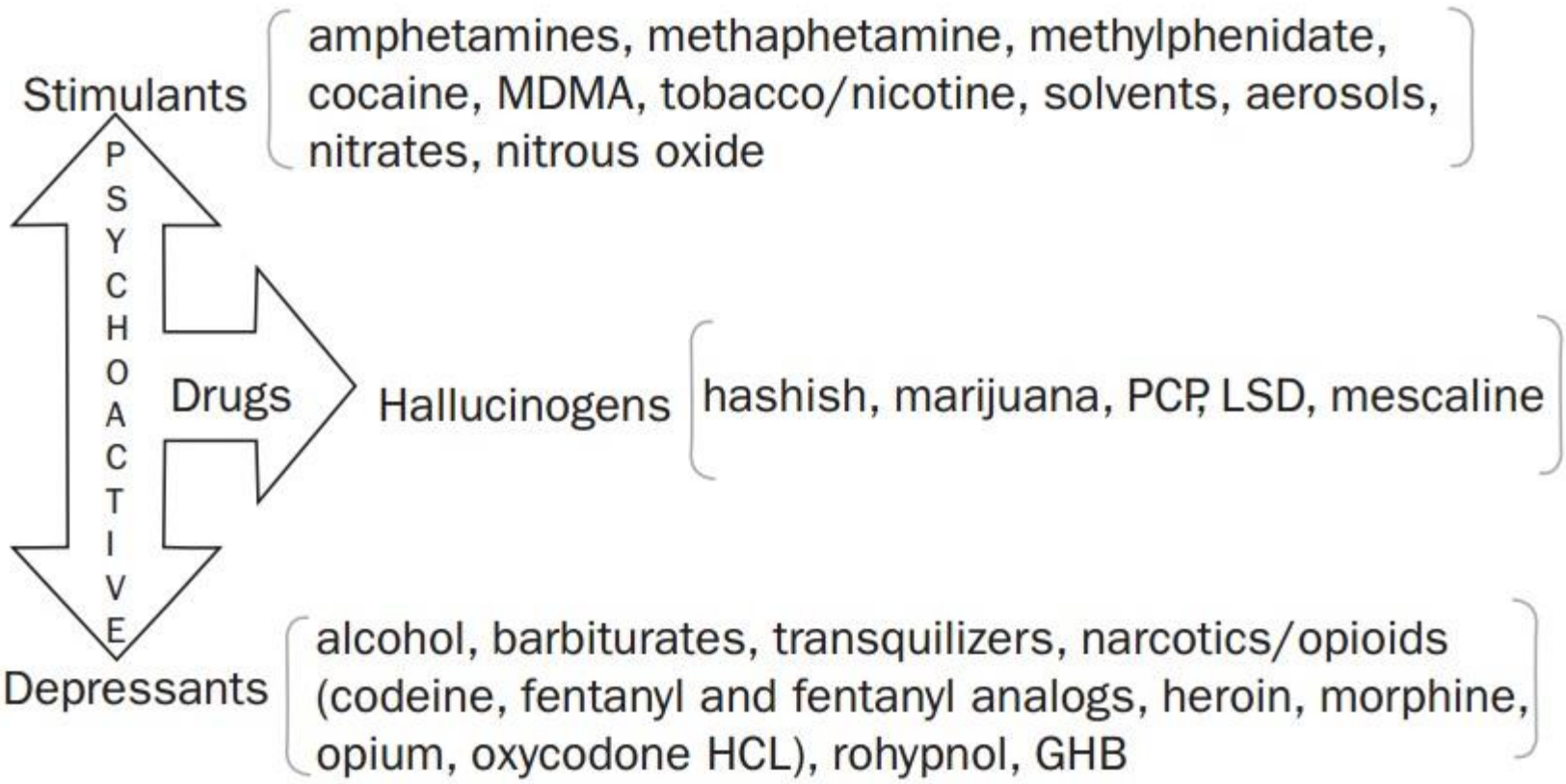
Websites

The most important international websites dedicated to counterfeit medicines:

- ✓ Business Action to Stop Counterfeiting and Piracy (BASCAP) (www.iccwbo.org/bascap)
- ✓ European Alliance for Access to Safe Medicines (EAASM) (www.eaasm.eu)
- ✓ German Pharma Health Fund (GPHF) (www.gphf.org)
- ✓ Global Congress on Combating Counterfeiting (www.ccapcongress.net)
- ✓ International Anti-Counterfeiting Coalition (IACC) (www.iacc.org)
- ✓ Pharmaceutical Security Institute (PSI) (www.psi-inc.org)
- ✓ BuySafeDrugs.info (www.buysafedrugs.info)

Abused Drugs

Abused drug – a drug used in a non-therapeutic way



Thank You !

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