

**FROM MOLECULES TO MEDICINES :  
AN IN-DEPTH LOOK INTO TODAY  
DRUGS**

***DR. NORSARWANY MOHAMMAD  
JABATAN PEDJATRJK  
PUSAT PENGAJJAN SAJNS PERUBATAN***

## **From Molecules to Medicines: An In-Depth Look Into Today Drugs**

### **1<sup>st</sup> Lecture**

#### **Overview by first speaker: Dr Alora ( Professor in Medicine and Bioethics, Phillipines)**

Speaker quoted a few cases where patient died following consumption of prescribed medicines:

Panama story: 365 people died following consumption of cough medicine. Investigation revealed harmful substances Diethylene Glycol which was substituted for glycerine.

Bohol story: A 41 year old lady died of uterine atony following the usage of Methylergometrin maleate

Questions: What is the PROBLEM? Something wrong with GENERIC formulation. Should everyone receive branded, ORIGINAL drugs?

What is the threat of **substandard** drugs?  
Patients must be protected?

### **2<sup>nd</sup> Lecture by Prof Palapac (Pharmacologist, Phillipines)**

#### **Title: Good Manufacturing Practice (GMP)**

Late 2007, Heparin products of Baxter

-causing allergic reaction in children: difficulty breathing, nausea

-350 patients affected

-Investigation showed contaminant: highly sulfated form of chondroitin

-home message: GMP non compliance

-conclusion: many factors in the manufacturing process affect quality of drugs

Factors affecting quality of drug

1. material
2. procedures
3. packaging
4. storage

Material

Expecting 100% purity

Impurity is the cause for side effects

Procedures

Different in bioequivalent of the product

## Packaging

Properties of drugs: clavulanic should not be wet , amoxicillin should not be dry

Drug is sensitive to the external environment

Hence appropriate protective packaging is important

## Storage

Storage condition affect drug stability

## 3<sup>rd</sup> Lecture

**Dr Suzette Lazo (Pharmacologist, Phillipines)**

## Drug Development

Discovery of drug molecules



Preclinical testing



Phase I



Phase II



Phase III

### Phase I

Involving 20-30 healthy volunteers

### Phase II

200-300 volunteers used to check efficacy and side effects of each drugs

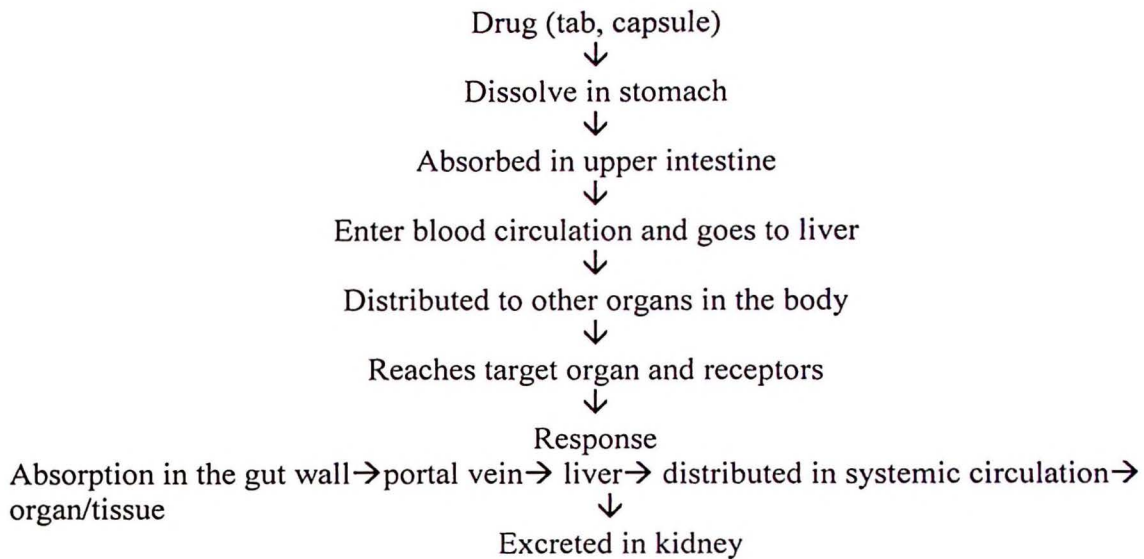
-Does it works in patients?

### Phase III

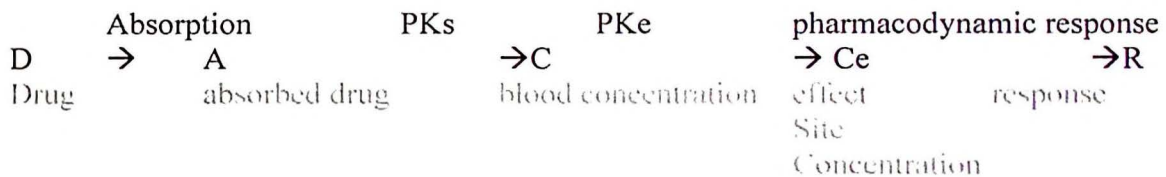
Is it safe and more effective versus the gold standard

1000-3000 patient volunteers used to monitor drug reaction in long term

## Basic principle



$D \rightarrow A \rightarrow C \rightarrow Ce \rightarrow R$



PKs= pharmacokinetic process

PKe= equilibrium process

## Bioavailability

Bioavailability is the rate and extent to which the active ingredient or active moiety is absorbed from the active site.

Supra-bioavailable → increase risk of ADRs

Sub-bioavailable → result in treatment failure

## Bioequivalence (BE)

Generic versus pioneer

Drug product change after approval versus product before the change

Alternative dosage form, eg immediate vs extended

New route of administration

Significant manufacturing change which may affect the bioavailability of a drug

**Types of BE studies**

- Pharmacologic end-point BE studies
- Clinical end-point BE studies
- Blood level BE studies
- Urine BE studies

**Definition of bioequivalent**

The absence of significant different in the rate and extent to which the active ingredient in pharmaceutical equivalent or pharmacologic alternatives become available at the site of drug action.

To be BE, 90% confident interval with AUC and Cmax of the test drug must fall within 80% to 125% of the reference standard (innovator).

Bioequivalent should be done for generic drugs.

**Parameter of BE study**

Eg :

Cmax

AUC

Confident interval 80-120%

**Characteristics of good drugs:**

Correct solution

Practice GMP

Testing for quality

Substandard drugs: fake, imported

**Quality versus substandard drugs**

Quality drugs	Substandard drugs
effective	harm
Save	ineffective
cure	dangerous

**HOW? WHAT TO DO WHEN YOU SEE NEW DRUGS**

1. Use good prescribing habits
  - know the patient, drug and law
  - demand to see objective and credible evidence
  - choose drugs wisely
  - monitor deligently
2. Learn and share learning
  - clinical and formulary experience research
3. educate others
  - patients, other healthcare providers, public
  - be aware and vigilant of substandard drugs

4. support effort of others  
-Hospital therapeutics committees  
-Government regulators

5. initiate alliances  
-form committees within your professional societies  
-influence advertising

**Prepared by Dr Norsarwany Mohamad, Dpt of Paediatric 8.4.2009**