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Subject: Physical Pharmacy (BP-403T)

Unit: V

Topic: Drug Stability

INTRODUCTION

STABILITY:

USP defines stability of pharmaceutical product as, "extent to which a product retains with in specified limits and throughout its period of storage and use (i.e. shelf life).

The capacity or the capability of a particular formulation in a specific container to remain with in particular chemical , microbiological , therapeutically , and toxicological specifications.

DRUG STABILITY

Drug stability is defined as the ability of the pharmaceutical dosage form to maintain the physical, chemical, therapeutic and microbial properties during the time of storage and usage by the patient.

The purpose of stability studies is to provide evidence on how the quality of the active substance or pharmaceutical product varies with time under the influence of a variety of environmental factor such as temperature, humidity and light

IMPORTANCE

Chemical and **physical degradation** of drug substances may change their **pharmacological effects,** which is then affecting on their **therapeutic** and **toxicological** effect.

Pharmaceuticals products are used **therapeutically** based on their **efficacy and safety**, they should be stable.

Maintenance of quality until the time of usage or until their **expiration date**.

The **quality** should be **maintained** under the various conditions that pharmaceuticals encounter, during production, storage in warehouses, transportation and storage in hospitals as well as in the home.

NEED


Quality varies with time
Safety point of view of patient
Shelf life of drug product
NEED OF STABILITY STUDIES
Essential quality attributes
Storage condition
Prevention of expenses
Container closure suitability

Where stability studies takes place.....

Drug discovery development

New chemical entity

Preclinical studies including:
- chemistry
- Physical properties
- Biological
  - i. Pharmacology
  - ii. ADME
  - iii. Toxicology
- Preformulation
  - i. Bulk characterization
  - ii. STABILITY ANALYSIS
  - iii. Solubility analysis

Clinical studies

Postmarketing

Types of stability

TYPES OF STABILITY TESTING

SR. NO.	STUDY	STORAGE CONDITION	TESTING TIMING (MONTH)	Minimum Time Period Covered By Data At Submission
1	**LONG TERM (Ambient)**	25° C ± 2° C 60%RH ± 5%	0, 3, 6, 9, 12, 18, 24, 36, 48, 60.	**12 months**
2	**INTERMEDIATE (controlled)**	30° C ± 2° C 60%RH ± 5%	0, 3, 6, 9, 12.	**6 months**
3	**ACCELERATED (Short term)**	40° C ± 2° C 75%RH ± 5%	0,1, 2, 3, 6, 9.	**6 months**

DEGRADATION PATHWAYS

Degradation of active drug leads to **lowering of quantity** of the **therapeutic agent** in the dosage form

A **toxic product formation** may takes place due to decomposition instability of drug product can lead to a decrease in its **BIOAVAILABILITY**.

Changes in **PHYSICAL APPEARANCE** of given dosage form may takes place.

Degradation may increase or decrease the **POTENCY** of drug.

TYPES OF DEGRADATION PATHWAYS

PHYSICAL

THERAPEUTIC

CHEMICAL

Degradation Pathways

TOXICOLOGIACAL

MICROBIOLOGICAL

PHYSICAL DEGRADATION

- LOSS OF VOLATILE COMPOUNDS
- LOSS OF WATER
- ABSORPTION OF WATER
- CRYSTAL GROWTH
- POLYMORPHISMS
- COLOUR CHANGES
- PHOTOLYSIS

CHEMICAL DEGRADATION

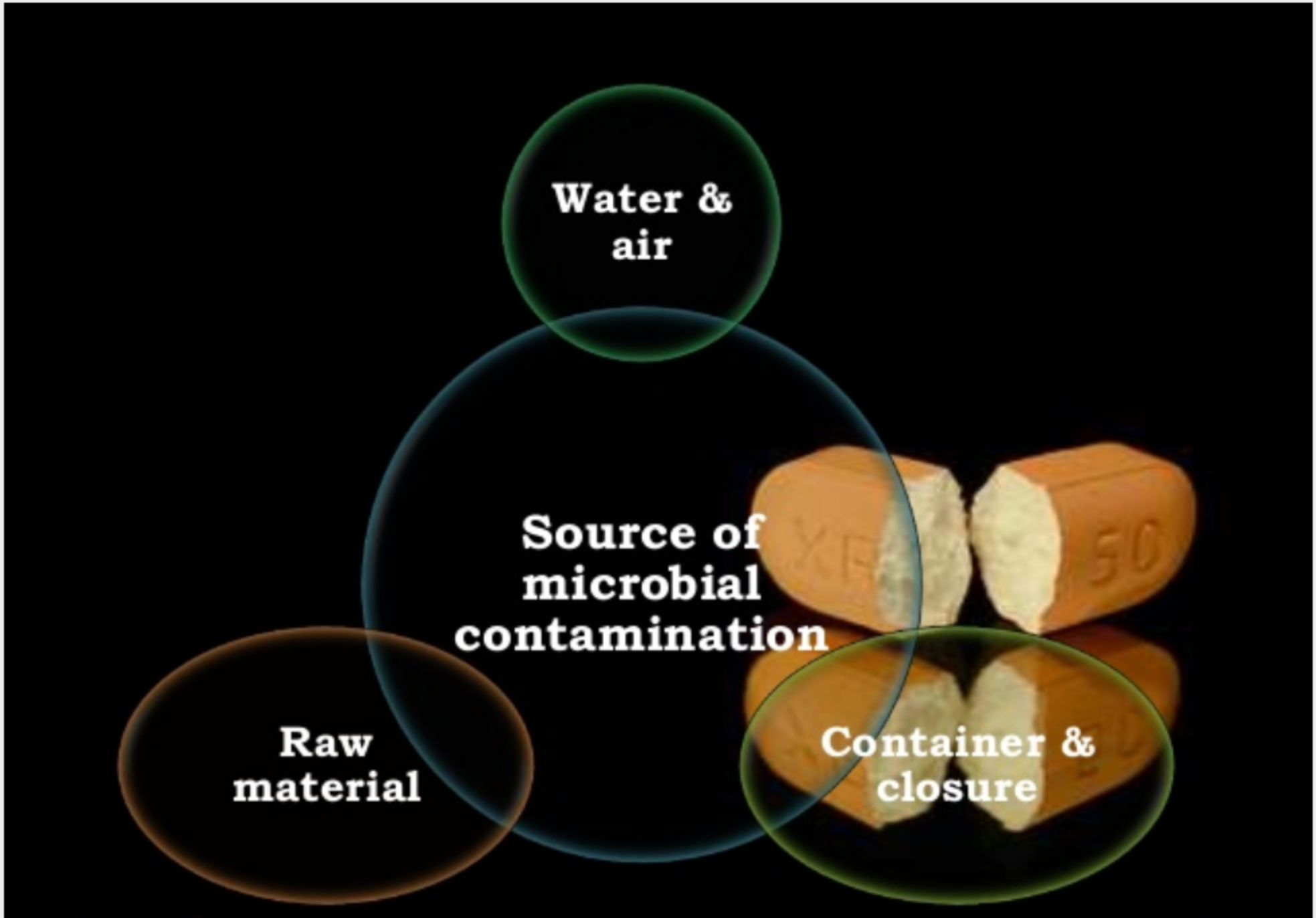
- HYDROLYSIS
- ISOMERIZATION
- RACEMIZATION
- EPIMERIZATION
- DECARBOXYLATION
- ELIMINATION
- OXIDATION

MICROBIAL DEGRADATION

Contamination of a product may sometimes cause a lot of damage and sometimes may not be anything at all.

-Thus it is dependent on the type of microbe and its level of toxicity it may produces.

-If parenterals or ophthalmic formulations are contaminated, it may cause serious harm.


Water &
air
Source of
microbial
contamination
Raw
material
Container &
closure

THERAPEUTIC DEGRADATION

Therapeutic effect must be changed due to hydrolysis, isomerisation or epimerization .

Example:

Adrenaline

Toxicological degradation

SOME DRUGS MAY PRODUCE TOXIC PRODUCT .

EXAMPLE:

TETRACYCLINE, CHLORAMPHENICOL