

## Spoilage and their type and treatment

The logo of Galgotias University is a circular emblem with a stylized 'G' shape in the center. The 'G' is composed of three curved segments in shades of yellow, blue, and red. The background of the emblem is a gradient of light blue and white.

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# DEFINITION

- The action or process of spoiling, especially the deterioration of food and other perishable goods.
- Any change which renders a product unacceptable for human consumption.
- Complex event in which a combination of microbial and biochemical activities may interact.
- One of the major reason that led to preservation.
- **MICROBIAL SPOILAGE:** This refers to damage to food, pharmaceutical products that is caused by micro organisms (bacteria, moulds and yeasts). Micro organisms can grow in almost all kinds of food products. As micro-organisms occur everywhere around us, there is always a risk of **microbial spoilage**.

# TYPES OF SPOILAGE

- MICROBIAL SPOILAGE
- NON-MICROBIAL SPOILAGE
- Based on rate of spoilage: There are three types-
  - Highly perishable: Meat, Fish, Egg, Milk, Most fruits and Vegetables.
  - Semi perishable: Potatoes, Some Apple Varieties, Nut meats.
  - Non-perishable or stable: Sugar, Flour, Dry Beans.
- PHARMACEUTICAL SPOILAGE

# PHARMACEUTICAL SPOILAGE

- Spoilage of pharmaceutical products and drugs are referred as the changes in the physical and chemical properties in such a way that the formulation or therapeutic agent gets deteriorate and become not suitable for use.
- Pharmaceutical product is a combination of two things:
  - 1.Active drug
  2. Formulation additives

If there is any change in their efficacy, action, etc. it is said to be spoiled product which can not be used.

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# PHARMACEUTICAL SPOILAGE

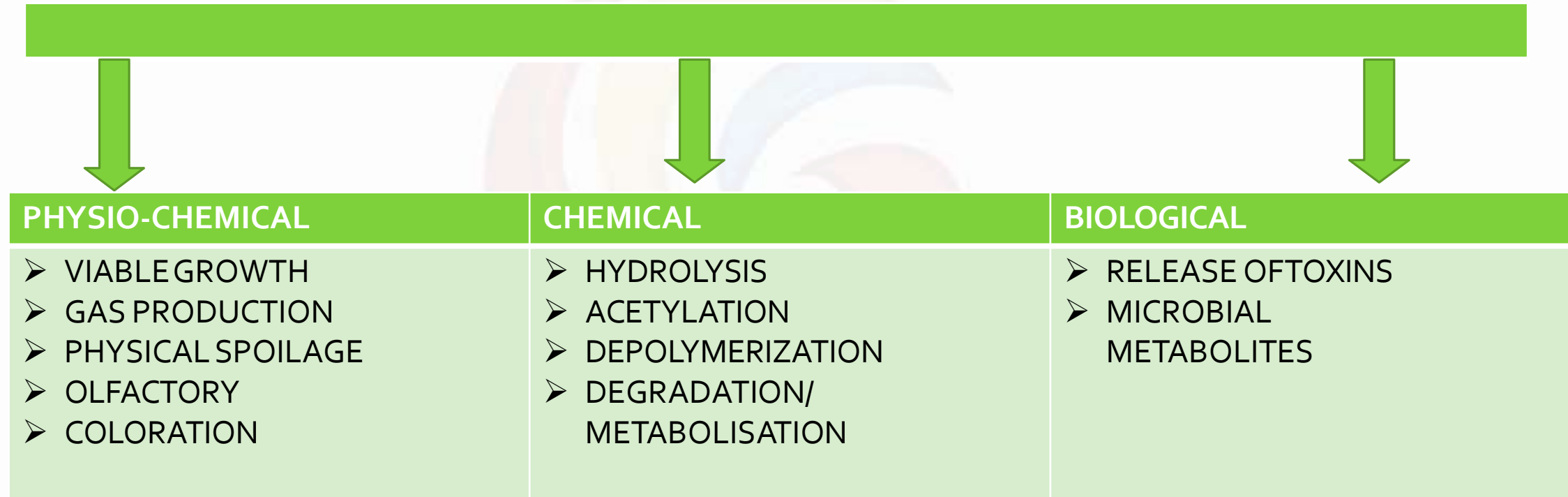
- There are several factors that cause pharmaceutical spoilage: Mainly, we study about microbial spoilage of pharmaceutical products.

<b>PHYSICAL</b>	<b>CHEMICAL</b>	<b>MICROBIAL</b>
Deterioration of pharmaceuticals due to physical factors like, heat, temperature, evaporation, etc.	Deterioration of pharmaceuticals due to chemical reactions like oxidation, reduction, hydrolysis, photolysis, ionization, etc.	Deterioration of pharmaceuticals due to contamination of any microbial cell like bacteria, fungi, moulds, etc.

# MICROBIAL SPOILAGE OF PHARMACEUTICALS

- Microbial spoilage includes the microbial contamination of pharmaceutical products with the microbes which lead to spoilage of product affecting the drug safety and quality and is not intended for use.
- Shortly, microbial spoilage of pharmaceutical products is the deterioration of pharmaceuticals with contaminant microbes.
- It decreases the stability and intensity of the product.

# TYPES OF MICROBIAL SPOILAGE



# PHYSIO-CHEMICAL

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In this kind of spoilage, there are some chemical changes are caused by microbial species and due to these changes the physical properties are also gets altered or deteriorate, thus it is called the physico-chemical spoilage.

**1.VIABLE GROWTH:** In this kind of spoilage, microbial cells form a visible layer over the surface of pharmaceutical formulations. This layer or the presence of microbial cell can be clearly seen by naked eyes.

**Example:** layer of moulds over syrups or sugar containing products, creams, ointments.

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**2. COLORATION:** Color change occurs due to the alteration in components of chemical nature, and these changes are caused by change in pH of the formulation, redox of the product, production of some other metabolites by microorganisms.

**Example:** Pseudomonas species microorganism metabolize wide range of metabolites that cause coloration of blue-green, brown.

Surface decoloration of tablets containing biological products by some moulds.

**3. GAS PRODUCTION:** Some microorganisms contaminants in pharmaceutical formulations produces gases by their metabolic activities and form gas bubbles and broth/foam over the formulation.

Formulations containing carbohydrates or starchy material are more susceptible for gas production.

**Example:** production of CO<sub>2</sub> in syrups caused by osmo- tolerant mould and yeasts.

Klebsiella produces gas in creams and ointments containing vitamins and proteins.

Desulphovibrio oxidise simple organic compounds and produces hydrogen sulphide in suspensions.



**4. PHYSICAL SPOILAGE:** These are some changes in physical appearance caused by microbial cell activities.

**Example:** In emulsions, some microbial cells cause hydrolysis of oil phase, cause change in oil-water equilibrium and make emulsion unstable. Hydrolysis of oils also affect pH of formulation and alter the stability of emulsions.

In syrups, microbial cells metabolise sugar molecules, and due to which the concentration of syrup change and product become unstable.

**5. Olfactory spoilage:** Spoilage by some organisms and moulds generates unpleasant smell from the product. This kind of spoilage mainly caused by microbial cells that produce sulphur containing gases [SO<sub>2</sub>, H<sub>2</sub>S] and fishy smell due to formation of fatty acids along with odour generated by amines and alcohol production.

**Example:** Contamination in syrup of Tolu by penicillin spp. Produces toluene like smell.

Actinomycetes produce smell of geosmine in water phase used for formulations.

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# CHEMICAL SPOILAGE

- There are various types of chemical spoilage in pharmaceutical compound, these occurs due to various types of chemical reactions, mediated by contaminating microorganisms.

**1.HYDROLYSIS:** Some bacterial cells contains enzymes that catalyse hydrolysis of pharmaceuticals.

- **Example:** Atropine hydrolysed by Pseudomonas bacteria.
- Aspirin hydrolysed by esterase producing bacteria. Gelatin hydrolysed by Bacillus and Clostridium species.

**2.ACETYLATION:** Some microorganisms cellular enzymes

- cause acetylation of drugs and cause loss of activity.

**Example:** Chloramphenicol acetylation caused by staphylococci and streptococci gram +ve bacteria by the enzyme chloramphenicol acetyltransferase.

**3.DEPOLYMERISATION:** It is a process in which the polymers are degraded to their monomers. A lots of polymers are used in formulation of many type of pharmaceutical preparations as diluents, binders, thickening, suspending agents, etc.

**Example:** Starch- depolymerize by bacterial amylase Pectin-  
depolymerize by bacterial pectinase

Dextran- depolymerize by bacterial dextranase

Cellulose- depolymerize by bacterial cellulase.

**4.DEGRADATION:** Due to the microbial contamination, the active therapeutic agents or the formulation ingredients can be degraded or metabolized.

**Examples:** Penicilin: degrade by batalactamase containing bacterial cells  
Fatty acids metabolized by some moulds Prednison degraded by aspergillus species bacteria.

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## **BIOLOGICAL SPOILAGE:**

- Some bacterial cells contaminated the pharmaceuticals and utilize the various compounds present in that formulation to perform their metabolic activities. Due to these metabolic activities, the microbial cells produce certain chemicals which they release in pharmaceutical preparations. This is called biological spoilage.
- Mainly two types of chemicals released by the microorganisms:
- **1. Microbial toxins 2. Microbial metabolites**



**MICROBIAL TOXINS:** Several microorganisms produce toxic molecules that may cause spoilage of pharmaceutical formulations. Such as endotoxins produced by some gram –ve bacteria like E.coli.

Exotoxins by clostridium botulinum.

**MICROBIAL METABOLITES:** Bacterial metabolites are the biosynthetic products from microbial cells. Bacterial cells produce various metabolites which cause product spoilage because these metabolites are toxic to humans.

Examples are different amines and organic acids from bacterial cells.  
Metabolites from fungi and moulds.

Fungi and moulds are more specifically grow on the formulations having Talc, kaolin, and starch.

# REASON OF CONTAMINATION

- The product gets contaminate due to various reasons like
  - Accidentally exposure to the environment**
  - Improper storage conditions**
  - Inadequate preparation of formulation**
  - Improper sterilization**

# FACTORS AFFECTING SPOILAGE OF PHARMACEUTICAL PRODUCTS

- By understanding the influence of environmental parameters on microorganisms, it may be possible to manipulate formulations to create conditions which are as unfavorable as possible for growth and spoilage, within the limitations of patient acceptability and therapeutic efficacy.
- The factors that affects the spoilage of spoilage:
  - **NUTRITIONAL FACTOR**
  - **MOISTURE CONTENT**
  - **REDOX POTENTIAL**
  - **STORAGE TEMPERATURE**
  - **pH**
  - **PACKAGING DESIGN AND DESIGN**

# ● **NUTRITIONAL FACTOR:**

- ❖ Presence of nutritional material enable or favours microorganisms to utilize these nutritional material as energy source and proliferate over pharmaceutical products.
- ❖ In any formulation the presence of vegetable/herbal extract or animal tissue or tissue extract provides nutritional support to microbial cells.
- ❖ Demineralized water[prepared by ion exchange method] also contain some nutritional material which support the growth of *Pseudomonas* bacteria.
- ❖ More complex formulation are more supportive for microbial growth.

## ● **MOISTURE CONTENT[Water Activity]**

- ❖ Microorganisms readily need water or moisture to grow. The presence of uncomplexed water in any formulation supports microbial growth. Greater the solute concentration, lesser the activity.
- ❖ When solutes dissolved in water they form hydrogen and other bonds with water and form complexed water, the free or unbounded water molecules are termed as uncomplexed water, and this uncomplexed water supports microbial growth.
- ❖ Condensed water film sometime accumulate over some dry pharmaceutical formulation like tablets or oils due to the storage in humid atmosphere, supports fungal i.e. *A.glaucus* and yeast growth.

CC MICROORGANISM	WATERACTIVITY
CLOSTRIDIUM BOTULINIUM	0.94
ESCHERICHIA COLI	0.93
SALMONELLA SPP.	0.94
SHIGELLA SPP.	0.96

- ❖ Moisture films over viscous syrups can also increase water activity and support growth of fungi and yeast.
- ❖ Some halophilic bacterial grows in high salt conditions.
- ❖ Minimal water activity for some microbial cells for growth.

# REDOX POTENTIAL:

- The oxidation-reduction or the Redox potential is defined as the ratio of the total oxidizing [electron accepting] power to the total reduction [electron donating power of substance], or in more easy way it's a property of any chemical to give or accept electrons.
- Microbial growth in any environment is influenced by its oxidation reduction balance i.e. redox reaction. Electron transfer is major factor for energy production. If the oxygen is present in any formulation, then this condition favours microbial growth, if any product gets infected by microbial cell.

## PACKAGING MATERIAL AND DESIGN:

- Packaging can have major influence on microbial contamination and spoilage of pharmaceuticals. Multi dose containers are more affected by microbial contamination because they are again and again exposed to environment when the drug is withdrawn from container.
- Wide opening mouth containers that contain formulations of vegetable oils, protein, vitamin, animal extracts, are readily contaminated as they provide large surface area exposure to the environment.



## Cont...

- **STORAGE TEMPERATURE:**
- The pharmaceutical formulation can be affected by microbial cell between the temperature range of  $-20^{\circ}\text{C}$  –  $60^{\circ}\text{C}$ .
- Below  $-20^{\circ}\text{C}$  almost no microbial contamination is observed and the same as above  $60^{\circ}\text{C}$ , microbial growth is suppressed. The reason for that is inactivation and denaturation of cellular enzymes, which are responsible for cell metabolic activities.
- Water for injection is stored at  $80^{\circ}\text{C}$  before preparation to minimize bacterial growth and to prevent bacterial activity to produce and release pyrogens to the water.

# pH of Pharmaceutical formulations:

- pH is represented as the potential of hydrogen ions. Some bacterial cells are grown better in acidic medium and some are in basic medium, this happens because in their favourable pH the enzymes of bacterial cells are more active to perform their metabolic activities.
- Some preparations of pH around 5-6 favour growth of moulds but inhibit bacterial growth.
- Some preparations having pH of 3-4 favour growth of moulds and yeast, i.e. fruit juice flavoured syrups.
- Some preparations of neutral pH like mouthwashes, distilled water, antacid preparations are contaminated by bacterial cells i.e. *Pseudomonas* spp.

- Basic pH formulations inhibit bacterial growth, i.e. magnesium and aluminium hydroxide gel, etc.
- Sometime primary fungal growth occurs in any product, these fungal cell metabolize the chemical and produce acids and raise the pH of formulations and favours secondary bacterial growth.



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