

UNIT-V

Spoilage



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RASMITA JENA
ASSISTANT PROFESSOR
SoPLS, CUTM, BBSR

- Types of spoilage
- Factors affecting the microbial spoilage of pharmaceutical products

Introduction

- Spoilage is **chemical and physicochemical degradation of pharmaceutical products** rendering it **unsuitable for use**.
- Spoilage is not desirable in pharmaceutical industry because deterioration of drugs and excipient occurs, as a result **product may lose its quality and it may become ineffective**. Entire batch may be required to be discarded.
- This **may cost huge loss** to the manufacturer. Moreover it **may attract litigation** from the consumers which **may cause huge financial loss** to the Company.

- Damaged products **may damage reputation of the manufacturing** company which may attract further financial loss.
- Microbial spoilage **may present potential health hazards to the consumers** like **toxicity , infection or even death**. Toxic metabolites may be produced **due to microbial growth** which may cause health hazards.
- Microbes **may deteriorate drugs** and thereby **reduce potency** of the medicament. There could be change in the appearance of the product like **decolourization, phase separation,** and **odour** formation etc.
- Following types of microbial spoilage occurs in pharmaceutical products.
 1. **Chemical spoilage.**
 2. **Physicochemical spoilage**
 3. **Biological spoilage.**

Chemical Spoilage

- **Chemical spoilage means deterioration of chemical nature of drugs and excipient.** Molecular structure of the ingredients may change.
- This change may affect physicochemical properties of the preparation. Potency of the drug may decrease.
- Further microbial growth may occur if chemical degradation of preservative occurs.
- Similarly chemical degradation of surfactants, organic polymers etc may damage specialized micro-environment for which they are used.
- Along with microbial contamination some -chemicals may also cause chemical spoilage like pesticide, disinfectants, bleaching agent, sanitizer etc. may add to chemical spoilage.

Physicochemical spoilage

- This type of spoilage may change physico-chemical properties of product. Following types of changes may occur.

i) Viable growth - Viable growth of microbes may occur inside the container. These growth may be visible in the form of floating layers, turbidity, humps, etc. Contamination of products by fungus species like *Aspergillus sp.* may cause this type spoilage. Some bacterial species may also show viable growth.

ii) Gas production -Some microbes may produce gas inside the containers. These gases may be visible in the form of bubbles, floccules etc. Contamination of products with bacteria like *E. coli* may produce gas if it contains sugars.

- iii) Coloration / Discoloration -Some microbes may decolorize formulation or it may produce unique colour which is different from the normal colour of the product.
- iv) Odor formation-Microbial growth in the finished product may produce bad odor or characteristic odor. It may produce a characteristic rotten smell.
- v) Taste change -Microbial spoilage may change the taste of the oral formulations. It may impart bitter or obnoxious taste to the oral formulation.

Biological Spoilage

- Spoilage of pharmaceuticals may produce some **undesirable** and dangerous molecule which has undesirable biological effects.
- Some microbes may produce toxins, pyrogen or other harmful metabolites.
- These biomolecules may be present in the product from the very beginning.
- Spoilage may occur, although no microbial contamination was there.

Factors affecting the microbial Spoilage of the Pharmaceutical products

- There are so many factors which affects Microbial spoilage. Some of these factors **reduce rate of spoilage** where as some factors **increases the rate of spoilage**.
- These factors are **related to nutritional requirement** of micro-organisms, environment and nature of micro-organism.
- There factors must be studied **to minimize the impact of spoilage**. Following factors affect the microbial spoilage of Pharmaceutical products.

i) Number of contaminating micro-organism

- There may not be sufficient spoilage if number of contaminants are less. This low level of contaminants **may not be able to multiply due to design of the formulation**. However during **long storage** these microbes **may cause damage**. If **initial contamination is high** then it may present an **undesirable challenge**.
- Products will be **damaged quickly** due to **presence of high numbers of microbes**.
- High level of contamination occurs due to **lapses in manufacturing process** or **due to high loads of contaminants in raw materials**.

ii) **Type of micro-organism**

- Some microorganisms are **more aggressive** than others. They **can quickly multiply** and **spoilage is much faster**.
- However, **aggressive microbes** may not **multiply initially** due to **presence of preservative** and other substances.
- Contamination of product with **natural communities** of **non-aggressive micro-organism** can facilitate **growth of other aggressive contaminants**.

iii) Presence of nutrients

- In product Micro-organism can utilize formulation components as nutrients and utilize these components for biosynthesis and growth.
- Many formulations may contain crude animal, vegetable and microbial products which creates a conducive environment for microbial growth and subsequent spoilage.
- Additives like sugar, amino acid, polyhydric alcohol may act as microbial nutrients. Primary contaminants may produce metabolites which could be used by aggressive microbes as nutrient.
- Demineralized water which is prepared by ion-exchange resins may contain nutrients.

iv) Presence of water

- Presence of water in formulation may promote microbial growth and subsequent spoilage. Uncompelled water or free excess water promotes this spoilage.
- Presence of free water may be measured by water activity. It is a ratio between vapor pressure of formulation and vapor pressure of water in similar condition.
- If water activity is 1 then it is conducive for microbial growth. Chances of microbial growth decreases with decrease in value of water activity. A value less than 0.88 is considered safe to prevent spoilage. However, some microbes can grow in extremely low water value condition. - *Aspergillus glaucus* can grow at a water activity value of 0.61.

v) Oxidation-reduction potential

- Contaminating micro-organism may require terminal electron acceptor to facilitate functioning respiratory pathway.
- Presence of dissolved oxygen increases redox potential of the product thereby promote microbial growth and spoilage.

vi) Temperature

- **Storage temperature is a great controller of microbial growth** and spoilage. However, spoilage may occur over a range -20°C to 60°C.
- Microbial growth and spoilage is less in low temperature and high temperature. Storing products at a cool place (8 °C to 12 °C) may cause negligible spoilage.
- High temperature can also prevent spoilage. Water for injection is stored above 80°C before filling and sealing. So extreme temperature can minimize spoilage.

vii) pH

- **Microbes prefer neutral pH for their growth. However some microbes** may prefer slightly acidic pH. Extremely acidic or alkaline pH of the formulation may prevent microbial growth and subsequent spoilage. Some communities of microbes can survive in extreme pH and change the pH, there by support growth of other micro-organism.

viii) Presence of protection materials

- **Some materials in formulation may protect** microbes during sterilization process. Polymers like gelatin, starch etc may increase microbial resistance to heat. Microbes may get adsorbed in particles and become more resistant to heat.

ix) Containers and packaging

- **Chances of contamination in single dose** ampoules and vials are negligible. However multi dose containers be contaminated by users themselves. Change in designs of these containers may minimize contamination and spoilage. Wide mouthed containers for creams and ointments are replaced by narrow mouthed tubes with screw cap closures.
- Multi dose injections are stored in containers which has self sealing rubber wads. Containers are sealed such a way so that it can prevent entry of water and oxygen to minimize water activity and redox potential.