



Preservation

- Agents that prevent the growth of micro-organisms in medicinal products.
 - Preparations that are most susceptible to microbial growth are most aqueous preparations including: **syrops**, **suspensions**, **emulsions**, and **semisolids particularly creams**.
 - Preparations containing **alcohol** may **not require preservatives**.
 - Most alcoholic preparations
 - Certain hydroalcoholic preparations
 - Generally, 15% V/V alcohol will prevent microbial growth in acid media and 18% V/V in alkaline media.
- ✧ **Spirits, tinctures, elixirs.**

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Preservative selection consideration

- The preservative prevents the growth of the type of m.o. considered the most likely contaminants of the preparation.
- The preservative is soluble enough in water.
- It does not affect on safety or causes any discomfort to the patient.

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Preservative selection consideration

- Stable with time.
- Does not interact with other ingredients.
- Does not interact with the container.
- **Undissociated** portion of the preservative in the pH of the preparation is the only portion effective against m.o.
 - The preservative selected must be largely undissociated at the pH of the formulation being prepared.

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Preservative selection consideration

- M.o. include molds, yeasts, and bacteria.
 - Bacteria generally favors a slightly alkaline medium
 - Molds and yeasts favor an acid medium.
- Few m.o. can grow below **pH 3** or above **pH 9**.
- Most aqueous pharmaceutical preparations are within the favorable pH range.
 - Therefore must be protected against microbial growth.

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Preservative selection consideration

- Acidic preservatives like **benzoic**, **boric**, and **sorbic acids** are more undissociated and thus more effective in acidic medium.
- Alkaline preservatives are less effective in acid or neutral media and more effective in alkaline media.

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Preservative

- The FDA recommends that:
 - Using the **lowest** effective concentration of an antimicrobial preservative
 - It should be demonstrated to be effective by an antimicrobial **preservative effectiveness test**.
 - The concentration used should be validated in terms of **efficacy** and **safety**, with the effectiveness confirmed to last throughout the intended **shelf life** of the product

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Mode of action of preservatives

- Preservatives interfere with microbial:
 - growth,
 - multiplication, and
 - metabolism
- 1. Modification of cell membrane permeability
- 2. Lysis and cytoplasmic leakage
- 3. Irreversible coagulation of cytoplasmic constituents
- 4. Inhibition of cellular metabolism
- 5. Oxidation of cellular constituents
- 6. Hydrolysis

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Examples

- **benzoic acid (0.1% to 0.2%),**
- **sodium benzoate (0.1% to 0.2%),**
- **alcohol (15% to 20%),**
- **phenol (0.1% to 0.5%),**
- **cresol (0.1% to 0.5%),**
- **phenylmercuric nitrate and acetate (0.002% to 0.01%),**
- **chlorobutanol (0.5%),**
- **benzalkonium chloride (0.002% to 0.01%),**
- **Combinations of methylparaben and propylparaben (0.1% to 0.2%), the latter being especially good against fungus.**
- The required proportion varies with the **pH**, **dissociation**, and other factors already indicated as well with the **presence** of other formulative ingredients with inherent preservative capabilities.

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Air displacement excipients

- Some drugs might be affected by air
 - Air contains oxygen
- Liquid filling under nitrogen is an effective measure for protecting the drug against oxidation.



Acidifying agents

- Used in liquid preparations to provide an acidic medium for product stability
- Examples:
 - Citric acid
 - Acetic acid
 - Fumaric acid
 - Hydrochloric acid