Fast Dissolving Tablets of Anti-Cholinergic Drugs: A Review

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***Abstract*- Fast dissolving tablets (FDTs) have emerged as a novel drug delivery system aimed at enhancing patient compliance, especially among pediatric, geriatric, and dysphagic populations. Anti-cholinergic drugs, which are primarily used to treat a variety of conditions such as gastrointestinal disorders, respiratory diseases, Parkinson's disease, and urinary incontinence, often present challenges in traditional dosage forms due to side effects and delayed onset of action. The development of FDTs for anti-cholinergic drugs addresses these issues by providing rapid drug disintegration and absorption, thus ensuring faster therapeutic action and improved bioavailability. This review provides a comprehensive examination of fast dissolving tablet technologies, including various formulation methods such as direct compression, lyophilization, sublimation, and melt granulation. It also covers evaluation parameters critical to FDT development, such as disintegration time, drug release profile, mechanical strength, and taste masking. A detailed analysis of current literature highlights recent advances in the formulation of anti-cholinergic FDTs and evaluates their therapeutic potential. The review concludes by discussing current challenges and future directions for optimizing these systems for clinical use.**

***Keywords*- FDT, ODT, Hysocine Butylbromide, API, COPD.**

I. INTRODUCTION

Oral drug delivery is the most preferred route of administration due to its ease of use, cost-effectiveness, and high patient compliance. However, conventional oral dosage forms such as tablets and capsules pose challenges for certain populations, particularly children, the elderly, and patients with neurological or swallowing disorders. In response, fast dissolving tablets (FDTs), also known as orally disintegrating tablets (ODTs), have been developed to offer rapid disintegration in the oral cavity without the need for water, providing a convenient alternative.

Anti-cholinergic drugs, which function by blocking the action of acetylcholine at parasympathetic sites in the smooth muscle, central and peripheral nervous systems, are widely used in the treatment of conditions such as chronic obstructive pulmonary disease (COPD), overactive bladder, Parkinson's disease, and gastrointestinal disorders. While effective, these drugs often require precise dosing and fast onset of action to be therapeutically efficient, especially in acute settings.

Traditional formulations of anti-cholinergic agents may lead to delayed therapeutic effects due to slower dissolution and absorption rates, and they may be associated with significant first-pass metabolism. Fast dissolving tablets provide a promising solution by enabling rapid drug release and absorption through the oral mucosa, potentially bypassing hepatic metabolism and improving systemic bioavailability.

This review focuses on the formulation and evaluation of fast dissolving tablets containing anti-cholinergic drugs. It explores the various types of FDTs, innovative formulation techniques, and essential quality control parameters. The article also presents a critical appraisal of existing literature to identify the therapeutic advantages, formulation challenges, and future perspectives in this area

ADVANTAGES OF FAST DISSOLVING TABLETS

Fast dissolving tablets offer several benefits over traditional dosage forms:

1. Rapid Onset of Action: FDTs dissolve quickly in the mouth, leading to faster absorption and onset of therapeutic effects.
2. Ease of Administration: They are particularly beneficial for patients who have difficulty swallowing pills, such as the elderly or pediatric populations.

3. Improved Patient Compliance: The convenience of FDTs can enhance adherence to medication regimens.
4. No Need for Water: FDTs can be taken without water, making them ideal for on-the-go use.

TYPES OF FAST DISSOLVING TABLETS

The types of FDTs can be broadly categorized based on their formulation approach and disintegration mechanism:

1. Conventional FDTs (direct compression-based)

These are the most commonly manufactured FDTs using standard tablet compression methods with superdisintegrants like crospovidone, sodium starch glycolate, or croscarmellose sodium. The formulation is optimized for rapid disintegration, often within 30 seconds, by incorporating hydrophilic excipients that swell upon contact with saliva.

Advantages:

- Cost-effective and easy to scale up
- Requires minimal processing steps
- Suitable for heat- and moisture-sensitive drugs

2. Lyophilized or freeze-dried tablets

These tablets are prepared by freezing the drug solution or suspension and removing the water through sublimation. This results in a porous, lightweight structure that disintegrates almost instantly in the mouth.

Advantages:

- Extremely fast disintegration (within 5–15 seconds)
- Suitable for fragile or low-dose drugs
- Enhanced patient acceptability

Limitations:

- Fragile and may require special packaging
- Expensive manufacturing process

3. Molded tablets

Prepared by molding a moist blend of drug and excipients into tablets, followed by drying. These tablets are generally softer and dissolve more quickly than compressed tablets.

Advantages:

- Fast dissolution due to porous structure
- Good mouthfeel and palatability

Limitations:

- Poor mechanical strength
- Not suitable for high-dose drugs

4. Sublimation-based tablets

This method involves incorporating volatile ingredients like camphor or menthol that are later sublimated, leaving behind a highly porous structure that promotes rapid disintegration.

Advantages:

- Improved tablet porosity
- Faster saliva penetration

Limitations:

- Requires precise temperature control
- May involve additional processing steps

5. Effervescent tablets

These FDTs include effervescent agents like citric acid and sodium bicarbonate that react with saliva to produce carbon dioxide, which facilitates tablet breakdown.

Advantages:

- Rapid disintegration via effervescence
- Enhanced drug solubility and taste masking

Limitations:

- Hygroscopic and moisture-sensitive
- Complex formulation requirements

II. MATERIAL AND METHODS TO FORMULATE FAST DISSOLVING TABLETS

Key Components

- Active Pharmaceutical Ingredient (API): The anti-cholinergic drug itself, which must be selected based on its solubility and stability.
- Superdisintegrants: These agents facilitate rapid disintegration of the tablet in the oral cavity. Common superdisintegrants include sodium starch glycolate and croscarmellose sodium.
- Binders: These help in maintaining the integrity of the tablet. Examples include polyvinylpyrrolidone (PVP) and hydroxypropyl methylcellulose (HPMC).
- Flavoring Agents: To improve palatability, especially for pediatric formulations.

Below are the major techniques used in FDT formulation:

1. Direct compression

Overview:

Direct compression is the most common and economical method for preparing FDTs. It involves mixing the active pharmaceutical ingredient (API) with superdisintegrants and other excipients, followed by compression into tablets.

Key Excipients:

- Superdisintegrants (e.g., crospovidone, croscarmellose sodium)
- Fillers (e.g., mannitol, microcrystalline cellulose)
- Lubricants (e.g., magnesium stearate)

Advantages:

- Simple and scalable
- Avoids moisture and heat exposure
- Suitable for moisture-sensitive anti-cholinergic drugs

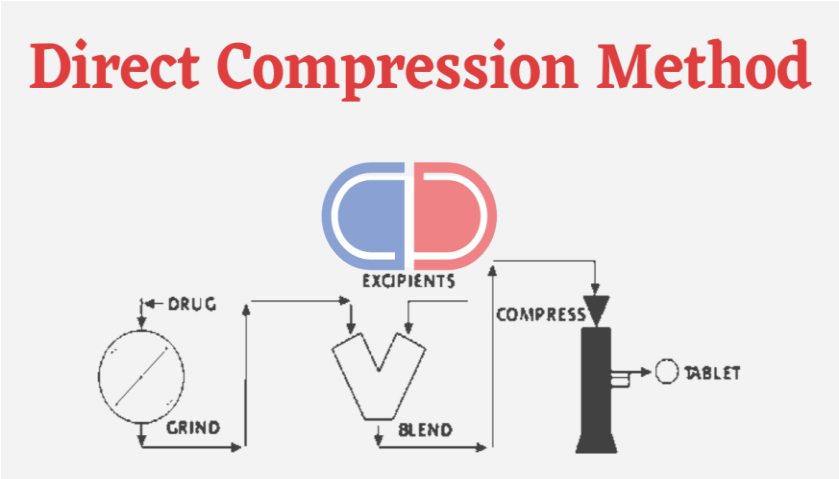

Fig. 1: Direct compression method

2. Lyophilization (freeze-drying)

Overview:

This method involves dissolving or suspending the drug in a suitable matrix solution, which is then frozen and subjected to sublimation to remove water. The resulting porous structure allows for extremely rapid disintegration.

Advantages:

- Ultra-fast disintegration
- Enhanced bioavailability

Limitations:

- High cost
- Fragile tablets that require specialized packaging

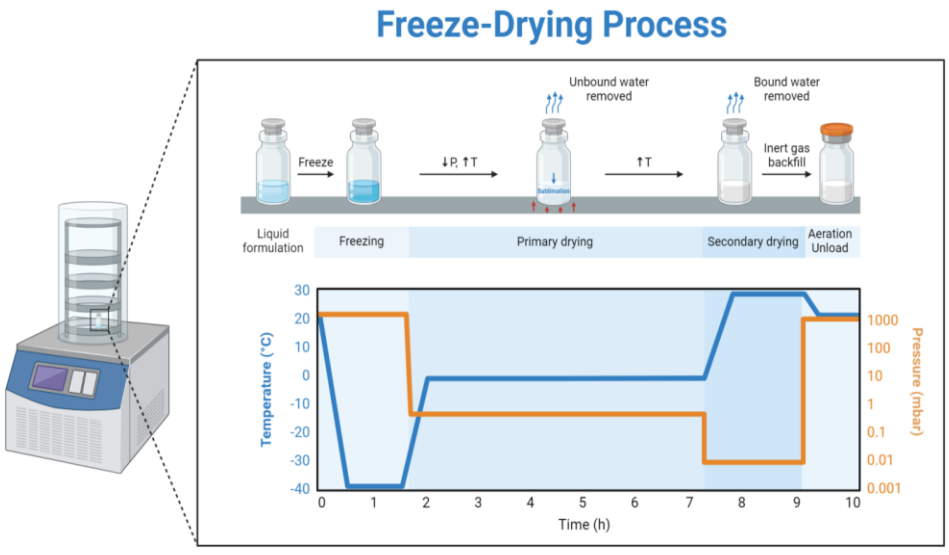

Fig. 2: Freeze Drying Process

3. Sublimation

Overview:

Volatile substances like ammonium bicarbonate, camphor, or menthol are added to the tablet blend and then sublimated during drying. This leaves a porous matrix that facilitates rapid disintegration.

Advantages:

- Enhanced porosity and saliva penetration
- Faster disintegration than direct compression

Limitations:

- Involves additional processing steps
- Precise control of sublimation conditions is needed.

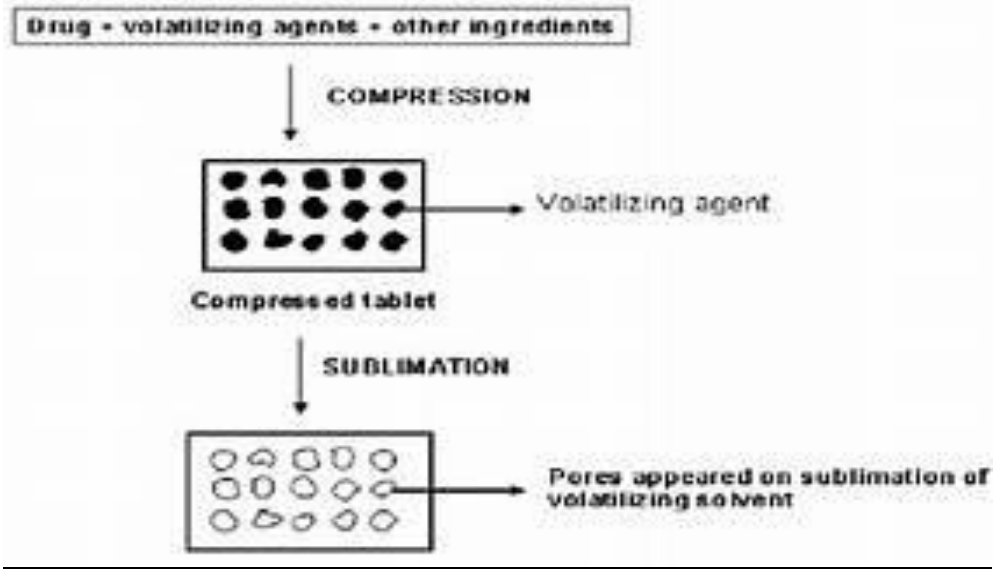

Fig. 3: sublimation method

EVALUATION OF FAST DISSOLVING TABLETS

The successful development of fast dissolving tablets (FDTs), particularly those containing anti-cholinergic drugs, relies on rigorous evaluation to ensure quality, safety, efficacy, and patient acceptability. Since FDTs are designed to disintegrate rapidly in the oral cavity, conventional tablet evaluation parameters are used alongside specialized tests focused on disintegration time, mouthfeel, and taste. Below are the key evaluation parameters for FDTs:

1) Pre Compression Parameters

1. Angle of repose

The angle of repose is a measure of the powder's flowability, which is crucial for uniform tablet production. It is the maximum angle at which a powder can remain stable on a heap without moving. A smaller angle indicates better flowability, while a higher angle implies poor flow.

- formula:
  $\tan(\theta)=\frac{h}{r}$
  Where:
  h = height of the powder cone,
  r = radius of the base of the powder cone.
- interpretation:
  - Angle < 30°: Excellent flowability
  - 30° - 40°: Good flowability
  - 40°: Poor flowability

Good flowability is crucial to ensure uniform filling of tablet molds during manufacturing, which directly impacts the quality of the final product.

2. Bulk density and tapped density

bulk density and tapped density are used to assess the packing and compressibility of the powder blend. These properties are essential to determine the flowability and the volume reduction after compression.

- bulk density (BD): The mass of powder divided by its volume before tapping (loose packing).
  $BD=\frac{\text{Mass of powder}}{\text{Volume of powder (untapped)}}$
- tapped density (TD): The mass of powder divided by its volume after tapping (closely packed).
  $TD=\frac{\text{Mass of}$

powder}}{\text{Volume of powder (tapped)}}TD=Volume of powder (tapped)Mass of powder

- importance:
  - A high bulk density means more drug can fit in a smaller tablet size.
  - A low tapped density suggests poor packing ability and lower tablet mass.

3. Carr's index (compressibility index)

The Carr's Index (CI) measures the compressibility of a powder and reflects the ease with which a powder can be compacted. This index helps determine how the powder will behave during tablet compression.

- Formula:
  Carr's Index=Tapped Density−Bulk DensityTapped Density×100\text{Carr's Index} = \frac{\text{Tapped Density} - \text{Bulk Density}}{\text{Tapped Density}} \times 100Carr's Index=Tapped DensityTapped Density−Bulk Density×100
- Interpretation:
  - < 10%: Excellent compressibility
  - 11-15%: Good compressibility
  - 20%: Poor compressibility (may lead to inconsistent tablets)

2.) Post compression parameters

1. Weight variation

Weight variation is an important test that helps assess the uniformity of the tablet mass. Tablets are randomly selected, weighed individually, and compared to the average tablet weight.

- Acceptance criteria (IP/USP):
  - ±10% deviation for tablets weighing < 130 mg.
  - ±7.5% deviation for tablets weighing 130–324 mg.
  - ±5% deviation for tablets > 324 mg.

Tablets must have consistent weight to ensure accurate dosing.

2. Hardness (kg/cm²)

Hardness (also called tablet crushing strength) refers to the force required to break a tablet. It is crucial for tablet handling, packaging, and transportation. FDTs should have sufficient hardness to prevent breakage during handling but not be so hard that they delay disintegration.

- optimal range: The hardness of FDTs should typically be between 2-4 kg/cm² to ensure they remain intact during handling but disintegrate quickly in the mouth.

3. Friability (%)

Friability measures the tablet's ability to resist mechanical stress during handling. Tablets are subjected to a tumbling test, and the weight loss is recorded.

- Formula:
  Friability=Initial weight−Final weightInitial weight×100\text{Friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100Friability=Initial weightInitial weight−Final weight×100
- Acceptance Criteria:
  - A friability of < 1% is generally acceptable for tablets, including FDTs, to ensure they are resistant to breakage and abrasion.

3.)Special evaluation parameters for FDTs

a) Disintegration time

- Key parameter for FDTs.
- Tablets should disintegrate within 30 seconds to 3 minutes in the oral cavity.
- Evaluated in simulated saliva or distilled water at 37 ± 0.5 °C.

b) Wetting time

- Time required for the tablet to become completely wet when placed on a moist surface.
- Short wetting time indicates rapid saliva penetration and faster disintegration.

c) Water absorption ratio

- Calculated to assess the ability of the tablet to absorb moisture and begin disintegration.
- Important for understanding saliva interaction.

III. RESULTS AND DISCUSSION

The results from various studies have highlighted the potential of FDTs to enhance the bioavailability and patient compliance of anti-cholinergic medications, with rapid disintegration times and improved therapeutic efficacy:

1. Disintegration time and drug release

One of the most significant characteristics of FDTs is their ability to disintegrate rapidly upon contact with saliva, which directly influences the onset of action of the drug. Studies such as those by Kumar et al. (2017) and Singh and Patel (2019) demonstrate that the incorporation of superdisintegrants like crospovidone and sodium starch glycolate effectively reduced the disintegration time of anti-cholinergic FDTs to under 30 seconds.

For example, FDTs formulated with *oxybutynin hydrochloride* showed rapid disintegration (13–17 seconds) when camphor was used as a subliming agent, creating a highly porous matrix. This quick disintegration translates into faster drug release, which is particularly beneficial for conditions requiring prompt relief, such as acute exacerbations of respiratory diseases or bladder spasms.

2. Taste masking

Taste is a critical factor in the development of FDTs, particularly for bitter drugs like anti-cholinergic agents. The success of FDTs in pediatric and geriatric populations, who may be more sensitive to unpleasant tastes, heavily depends on the effectiveness of taste-masking strategies.

Several studies have focused on overcoming this challenge. Mehta et al. (2020) used a combination of sweeteners and flavoring agents such as sucralose and mint to mask the bitterness of *ipratropium bromide*, resulting in improved palatability and patient compliance. Additionally, ion-exchange resins such as Kyron T-104 were successfully employed to encapsulate and mask the bitter taste of drugs like *tolterodine tartrate* (Sharma et al., 2018). These strategies have demonstrated promising results in reducing bitterness without compromising the release and efficacy of the drug.

Taste-masked FDTs not only enhance patient compliance but also improve the overall therapeutic experience, making them suitable for patients who require frequent dosing or those with difficulty swallowing conventional tablets.

IV. CONCLUSION

The development of fast dissolving tablets (FDTs) for anti-cholinergic drugs represents a significant advancement in oral drug delivery systems, offering numerous benefits in terms of patient compliance, rapid onset of action, and enhanced bioavailability. FDTs have proven to be an effective alternative to traditional tablets, particularly for patients with swallowing difficulties, the elderly, and pediatric populations, all of whom often struggle with conventional dosage forms.

Several formulation techniques, such as direct compression, lyophilization, sublimation, and the use of effervescent agents, have been explored to optimize the disintegration time, drug release, and mechanical strength of FDTs. Notably, the incorporation of superdisintegrants and taste-masking agents has proven essential for enhancing patient acceptability, especially given the bitter taste of many anti-cholinergic drugs. Techniques such as 3D printing and the use of natural excipients also hold promise for further enhancing the functionality and sustainability of FDTs.

Pharmacokinetic studies have confirmed that FDTs of anti-cholinergic drugs can lead to faster absorption and onset of action, which is particularly beneficial in conditions like chronic obstructive pulmonary disease (COPD), overactive bladder, and irritable bowel syndrome, where prompt therapeutic intervention is crucial. The improved bioavailability observed with FDT formulations also supports their potential for reducing side effects associated with first-pass metabolism.

In conclusion, fast dissolving tablets of anti-cholinergic drugs represent a promising and evolving area of pharmaceutical innovation. With continued research and development, FDTs are poised to provide an effective, patient-friendly, and fast-acting delivery system for anti-cholinergic medications, ultimately improving patient outcomes and quality of life.

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