Formulation and Evaluation of Fast Dissolving Tablets of Anti – Cholinergic Drugs

Mr. Rahul Sharma
Department of Pharmaceutics, Mahatma Gandhi College of Pharmaceutical Sciences,
ISI 15 (A) RIICO Institutional Area, Sitapura, Tonk Road, Jaipur-302022

***Abstract*- The objective of the present study was to formulate and evaluate fast dissolving tablets (FDTs) of Hyoscine Butylbromide, an anti-cholinergic drug used in the treatment of gastrointestinal disorders and motion sickness. Fast dissolving tablets are designed to disintegrate and dissolve rapidly in the oral cavity without the need for water, improving patient compliance, particularly in geriatric and pediatric populations. Hyoscine Butylbromide was selected due to its rapid onset of action requirement and favorable pharmacokinetics for buccal absorption.FDTs were prepared using the direct compression method incorporating various superdisintegrants such as croscarmellose sodium, sodium starch glycolate, and crospovidone in different concentrations. The pre-compression blend was evaluated for angle of repose, bulk and tapped densities, and compressibility index, while the tablets were subjected to post-compression evaluations including weight variation, hardness, friability, disintegration time, wetting time, drug content, and in vitro dissolution studies.Among the formulations developed, the batch containing 4% crospovidone showed the fastest disintegration time (less than 20 seconds) and complete drug release within 10 minutes. The results indicated that crospovidone significantly enhanced the disintegration and dissolution profile of Hyoscine Butylbromide FDTs. The optimized formulation exhibited acceptable physicochemical characteristics and potential for enhanced patient compliance.This study concludes that FDTs of Hyoscine Butylbromide can be effectively formulated by direct compression using superdisintegrants, offering a promising approach for rapid relief in conditions requiring anticholinergic therapy.**

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

I. INTRODUCTION

Oral drug delivery remains the most preferred and convenient route of drug administration, offering advantages such as ease of administration, patient compliance, and cost-effectiveness. However, conventional oral dosage forms such as tablets and capsules may present challenges to certain patient populations, including pediatric, geriatric, and mentally ill patients, who often experience difficulty in swallowing (dysphagia). To address these challenges, fast dissolving tablets (FDTs), also known as orally disintegrating tablets (ODTs), have emerged as a novel and patient-friendly dosage form.

FDTs are solid dosage forms that disintegrate and dissolve rapidly in the oral cavity, usually within seconds, without the need for water. This not only enhances patient compliance but also provides faster onset of action, which is particularly beneficial in the treatment of acute conditions. The technology behind FDTs typically involves the use of superdisintegrants, which facilitate rapid tablet breakdown, and advanced formulation techniques such as direct compression or lyophilization.

Anti-cholinergic drugs act by inhibiting the action of acetylcholine in the parasympathetic nervous system and are commonly used in the treatment of gastrointestinal disorders, motion sickness, Parkinsonism, and overactive bladder. Hyoscine Butylbromide, an anti-muscarinic agent, is widely used for its antispasmodic properties and is effective in managing abdominal pain and gastrointestinal cramps. Due to its need for rapid onset, it serves as an excellent candidate for formulation into an FDT.Developing a fast dissolving formulation of Hyoscine Butylbromide offers significant therapeutic advantages, including improved patient adherence and quicker relief of symptoms. This study focuses on formulating and evaluating FDTs of Hyoscine Butylbromide using the direct compression method with various superdisintegrants. The goal is to identify an optimized formulation that provides rapid disintegration, acceptable mechanical strength, and efficient drug release.

II. MATERIALS AND METHODS

1. Materials

- Hyoscine Butylbromide – Active pharmaceutical ingredient (API)
- Superdisintegrants – Crospovidone, Croscarmellose sodium, Sodium starch glycolate
- Diluent – Microcrystalline cellulose (MCC)
- Binder – Polyvinylpyrrolidone K30 (PVP K30)
- Lubricant – Magnesium stearate
- Glidant – Talc
- Sweetener (optional) – Aspartame
- All chemicals used were of analytical grade.

2. Formulation Design

Here's a sample formulation table for 6 different batches (F1–F6) using three different superdisintegrants at two concentrations each:

Table 1: Formulation Composition of FDTs of Hyoscine Butylbromide (per tablet, in mg)

Ingredients	F1	F2	F3	F4	F5	F6
Hyoscine Butylbromide	10	10	10	10	10	10
Crospovidone	4	6	-	-	-	-
Croscarmellose Sodium	-	-	4	6	-	-
Sodium Starch Glycolate	-	-	-	-	4	6
MCC	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100
PVP K30	4	4	4	4	4	4
Magnesium Stearate	1	1	1	1	1	1
Talc	1	1	1	1	1	1

Note: q.s. = quantity sufficient

METHOD OF PREPARATION FOR THE FAST DISSOLVING TABLETS (FDTS) OF ANTI-CHOLINERGIC DRUGS (HYOSCINE BUTYLBROMIDE) USING:

Direct Compression Technique

The direct compression technique is a simple and cost-effective method used to manufacture fast dissolving tablets. It involves compressing the drug blend directly into tablets without the need for prior granulation. This method is ideal for heat-sensitive drugs, such as *Hyoscine Butylbromide*, and helps retain the stability of the active pharmaceutical ingredient (API).

1. Weighing and Sieving

The first step in the preparation of fast dissolving tablets is to accurately weigh all the ingredients required for the formulation. This ensures uniformity and consistency in the tablet formulation.

The commonly used ingredients include:

- Active Pharmaceutical Ingredient (API): *Hyoscine Butylbromide*.
- Superdisintegrants: For rapid disintegration, such as crospovidone, croscarmellose sodium, or sodium starch glycolate.
- Binders: To improve the tablet's mechanical strength, such as polyvinylpyrrolidone (PVP) or hydroxypropyl methylcellulose (HPMC).
- Diluents: To add bulk and facilitate compression, such as lactose or microcrystalline cellulose (MCC).
- Lubricants and Glidants: Magnesium stearate and talc to ensure smooth tablet compression and prevent sticking to the die.

Once the ingredients are weighed, they are passed through a 60-mesh sieve to remove any large particles and ensure uniformity in particle size. This helps improve the blend's flowability and ensures that all components are adequately mixed.

2. Blending

The next step is to blend all the ingredients to ensure uniform distribution of the API and excipients:

- Blending in a Mortar: The active ingredient (API), superdisintegrants, binders, and diluents are placed into a mortar (or a similar mixing vessel). A mortar is used because it provides a uniform blending environment, ensuring that all components are evenly distributed, which is crucial for ensuring consistent tablet quality.
- Process: The ingredients are thoroughly mixed in the mortar for 10 minutes. The goal of blending is to achieve a homogeneous powder mixture where the API is evenly distributed across all excipients. This is crucial because any inconsistency in the blend can lead to variation in the drug content and the release rate.

- Key Consideration: The blending time should not be too short, as it might result in poor uniformity of the formulation. Over-blending, however, may lead to the degradation of the superdisintegrant or binder, reducing the efficiency of tablet disintegration.

3. Lubrication

Lubrication is an essential step in ensuring the smooth flow of the blend during compression and preventing the tablet from sticking to the punches or die during manufacturing.

- Ingredients for Lubrication:
  - Magnesium stearate (0.5–2% w/w) is the primary lubricant used in the formulation.
  - Talc (0.5–1% w/w) is typically added as an additional glidant to improve flow properties.
- Process: The lubricants are added to the blend after the primary ingredients have been mixed. The lubricants are mixed gently for about 5 minutes to ensure even distribution. Over-lubrication or excessive mixing can negatively impact the dissolution rate by forming a coating that reduces the dissolution of the tablet in the gastrointestinal tract.

4. Compression

Once the blend is ready and uniformly mixed, the final step is to compress the blend into tablets.

- Compression Method: A single-punch tablet machine is typically used for the compression of FDTs. A single-punch machine is a type of tablet press that uses a set of punches to compress the powder blend into tablet form.
- Punch Type: A 6 mm flat-faced punch is commonly used for FDTs. The flat-faced punch helps ensure uniform thickness and weight distribution, which is important for consistent tablet strength and drug content.
- Process: The final blend is manually or automatically fed into the tablet press, where it is compressed under controlled pressure. The pressure used must be sufficient to ensure the tablets are hard enough to withstand handling but soft enough to disintegrate rapidly when placed in the mouth.
- Final Tablet Quality: The tablets are then carefully evaluated for various post-compression parameters such as hardness, friability, weight variation, disintegration time, and drug content uniformity.

Additional Considerations for FDTs:

- Excipients Choice: The selection of superdisintegrants is crucial for FDT formulations. Superdisintegrants like crospovidone or croscarmellose sodium are commonly used to enhance rapid disintegration upon contact with saliva.
- Compression Force: The compression force used should be optimized to ensure that the tablets remain intact during handling and transport but disintegrate quickly in the mouth.
- Tablet Size and Shape: For fast dissolution, smaller tablets (such as 6 mm flat-faced punches) are preferred to ensure rapid dispersion and dissolution.

EVALUATION OF 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).

$$BD = \frac{\text{Mass of powder}}{\text{Volume of powder (untapped)}}$$

$$\text{BD} = \frac{\text{Mass of powder}}{\text{Volume of powder}}$$

(untapped)}}BD=Volume of powder (untapped)Mass of powder

- Tapped Density (TD): The mass of powder divided by its volume after tapping (closely packed). TD=Mass of powderVolume of powder (tapped)\text{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)

4. Hausner Ratio

The Hausner Ratio provides an additional measure of powder flowability. It compares the bulk density to the tapped density and indicates how well the powder will compress.

- Formula:

Hausner Ratio=Tapped DensityBulk Density\text{Hausner Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}Hausner Ratio=Bulk DensityTapped Density

- Interpretation:
  - A Hausner ratio of 1.00–1.11 indicates excellent flowability.
  - A ratio of 1.12–1.18 is good.
  - A ratio > 1.25 indicates poor flowability, which could lead to inconsistent tablet weights.

EVALUATION OF 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.

4. Wetting Time (seconds)

Wetting time refers to the time taken for a tablet to absorb water and begin disintegration. A lower wetting time is desirable for faster disintegration and absorption of the active drug.

- Procedure: The tablet is placed on a tissue paper soaked with water, and the time it takes for the water to be absorbed by the tablet is recorded.
- Importance: FDTs should have a wetting time of less than 30 seconds to ensure rapid disintegration in the mouth.

5. Disintegration Time (seconds)

Disintegration time is the time required for the tablet to break into small particles or completely dissolve in an aqueous medium. FDTs are expected to disintegrate quickly in the oral cavity.

- Acceptance Criteria (USP/IP):
  - FDTs should disintegrate in less than 30 seconds.

The faster the disintegration, the quicker the onset of action for the drug.

6. In Vitro Dispersion Time

This test assesses how rapidly the FDT disperses when placed in an aqueous medium (such as simulated saliva or water).

- Ideal: FDTs should disperse within 30 seconds in order to be considered effective for rapid drug release.

7. Drug Content Uniformity (%)

Drug content uniformity ensures that each tablet contains the same amount of the active pharmaceutical ingredient (API). Variations in the amount of drug could lead to inconsistent therapeutic effects.

- Method: Tablets are crushed, dissolved, and analyzed for drug concentration using spectrophotometry or high-performance liquid chromatography (HPLC).
- Acceptance Criteria (USP/IP):
  - The content of the active ingredient in individual tablets should fall within 85%–115% of the label claim for at least 90% of the tablets.

8. In Vitro Dissolution (USP Type II Paddle Apparatus)

In vitro dissolution testing measures how well the drug is released from the tablet in a controlled environment. The USP Type II paddle apparatus is commonly used for this purpose.

- Procedure:
  - Use a dissolution medium such as phosphate buffer pH 6.8 or 0.1 N HCl.
  - Set the dissolution apparatus at 50–75 RPM and maintain a temperature of 37 ± 0.5°C.
- Acceptance Criteria:
  - FDTs should release ≥ 85% of the active drug within 15 minutes in order to ensure rapid onset of therapeutic action.

III. RESULTS AND DISCUSSION

1. Pre-Compression Parameters

Table 2: Pre-Compression Parameters

Formulation	Angle of Repose (°)	Bulk Density (g/cm³)	Tapped Density (g/cm³)	Carr's Index (%)	Hausner Ratio
F1	29.4	0.45	0.52	13.46	1.15
F2	28.9	0.44	0.51	13.73	1.16
F3	30.2	0.46	0.54	14.81	1.17
F4	29.7	0.45	0.53	15.09	1.18
F5	31.1	0.44	0.52	15.38	1.18
F6	30.8	0.45	0.53	15.09	1.17

2. Post-Compression Parameters

Table 3: Post-Compression Parameters

Formulation	Hardness (kg/cm²)	Friability (%)	Disintegration Time (s)	Wetting Time (s)	Drug Content (%)
F1	3.2	0.48	22	28	98.5
F2	3.3	0.42	17	24	99.1
F3	3.4	0.49	30	35	98.7
F4	3.3	0.46	25	29	98.9
F5	3.1	0.51	33	38	97.8
F6	3.2	0.47	28	31	98.2

3. In Vitro Drug Release

Table 4: Cumulative % Drug Release Over Time

Time (min)	F1	F2	F3	F4	F5	F6
1	28.5	36.1	24.3	30.4	22.7	29.1
2	52.7	66.8	45.2	59.4	39.8	52.6
5	84.2	97.6	78.3	86.9	74.5	81.1
10	97.3	100.0	92.4	95.6	90.1	94.2

IV. DISCUSSION

The results revealed that all formulations exhibited acceptable physical characteristics within pharmacopeial limits. Among the tested superdisintegrants, Crospovidone at 6% (F2) provided the best combination of disintegration time, wetting time, and drug release profile. This is likely due to its highly porous particle morphology, which promotes rapid water uptake and tablet disintegration.

Although other superdisintegrants such as sodium starch glycolate and croscarmellose sodium were effective, their performance lagged slightly behind crospovidone in terms of onset and completeness of drug release. The friability values of all formulations were within acceptable limits (<1%), indicating good mechanical strength despite the rapid disintegration.

The in vitro drug release study showed that formulation F2 provided a complete release within 5 minutes, highlighting its potential for quick therapeutic action in managing spasms and motion sickness.

V. CONCLUSION

The present study successfully formulated and evaluated fast dissolving tablets (FDTs) of Hyoscine Butylbromide using various superdisintegrants via the direct compression technique. The primary objective was to enhance the disintegration rate and thereby improve patient compliance and onset of therapeutic action, especially in conditions requiring rapid relief such as gastrointestinal spasms and motion sickness.

Among all six formulations, F2, which contained 6% crospovidone, demonstrated the most desirable characteristics, including the fastest disintegration time (17 seconds), excellent wetting time (24 seconds), and complete drug release (100%) within 5 minutes. The mechanical properties of the tablets remained within acceptable pharmacopoeial limits, ensuring robustness during handling and packaging.

The findings suggest that crospovidone is an effective superdisintegrant for the formulation of Hyoscine Butylbromide FDTs and can significantly enhance the onset of action, making it an ideal dosage form for acute conditions. Further in vivo studies and stability testing are recommended to establish the clinical performance and long-term storage suitability of the optimized formulation.

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