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# Formulation and evaluation of mouth dissolving oral film for Drooling

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**Abstract**

Drooling also known as sialorrhea refers to unintentional loss of oral material from the mouth, such as saliva. The aim of this work was to develop a fast-acting mouth-dissolving benzhexol HCl thin film that would minimize drooling. It has a low oral bioavailability and is a strong drooling regulator in children with cerebral palsy. Many people find it challenging to swallow conventional dosage forms such as capsules and tablets. A fast-dissolving oral film was developed to help with all of these issues and to increase the bioavailability of medications. mouth films disintegrate quickly with medications, and the majority of medications enter the systemic circulation via the mouth mucosa. Oral films from the optimum batch dissolve in 20 seconds. Additional evaluations were conducted for the optimum film, including drug concentration, folding durability, pH values, disintegration duration, percentage elongation, and appearance.

**Key words :** Poor saliva control, Drooling, Hypersalivation, sialorrhea.

Oral film delivery is becoming a more advanced alternative to traditional delivery methods. When taken as prescribed, the solid oral film dosage form dissolves. The oral films can be taken without chewing or with water[5]. About 52% of the drug delivery industry is made up of the oral delivery market; the development of oral dose formulations with modified release has garnered a lot of interest. However, there are a few issues that are frequently linked to the oral administration of medications, such as reducing the possibility of partial API loss from crushing tablets or capsules or inaccuracy in liquid dose

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administration leading to overdosing or inefficiency in drug therapy[6,13,25] Fast-dissolving drugs delivery systems are gaining popularity to overcome these problems. These films disintegrate fast on tongue and releasing flavour[4,17,18].

Water or measurement are not needed as the drugs dosage is consumed. Due to its high vascularization and permeability, the oral mucosa's ability to absorb drugs into the systemic circulation is an attractive approach. Fast-dissolving films are the recommended oral dose form for many drugs due to their wide surface area, allowing for faster disintegration and improved patient compliance.

The formulation of the Benzhexol HCL mouth dissolving oral film, HPMC E5 or PEG 400 are used as plasticizer and film-forming polymers. Water is used as a solvent and sodium sucrose as the sweetener[15,24].

Trihexyphenidyl, also known as benzhexol, is an anti-muscarinic muscle relaxant that is prescribed as an antispasmodic medication for children's drooling control and movement disorders (dystonia). Trihexyphenidyl (Benzhexol) lowers dystonic movements and relaxes stiff, dystonic muscles in people with dystonia. The use of benzhexol hydrochloride to reduce drooling was tested on children with cerebral palsy. Before starting therapy, drooling was monitored, and the results were repeated until the ideal dosage of benzhexol hydrochloride was reached[19].

*Materials :* Benzhexol HCL was purchased Harman from Finochem Ltd is located at MIDC Industrial Area, Chilkalthana, sambhajinagar, Maharashtra, India. B.R.D.H. Scientific Suppliers, Nagpur, provided the HPMC.

*Preparation of MDF :*

Solvent casting is the method used to make the oral dissolving film for Benzhexol HCL. A film former is made with HPMC E5. PEG 400 was added, which is a flavouring, sweetening, and plasticizer[11].

*Method of preparing MDF :* Solvent casting process was used to make the benzhexol HCl mouth dissolving film. Separate HPMC E5 and E15 grades are a polymer used to make film. Plasticizers were used, including glycerol and polyethylene glycol 400 (PEG 400). After accurately calculating film-forming polymer, it was mixed with sufficient water to dissolve it. After that agitation was performed using a magnetic stirrer. it until the polymer was completely dissolved. Other materials, including the solubilizing agent sodium lauryl sulphate, PEG 400, and glycerol, sodium saccharin (a sweetening agent), and benzhexol HCl, were dissolved in the water that was left. A magnetic stirrer was used to mix the two liquids completely until they were homogenized, and then water was added to get the volume up to 10 millilitres.

After being transferred to a glass Petri plate, this solution was left to dry for a full day at room temperature[5,16]. When the film was cast on a petri plate, it was gently flaked off and cut into the right size and shape.as seen in figures 1 and 2.

HPMC E5
Fig. 1

HPMC E15
Fig. 2

Table-1. Composition of Mouth Dissolving Film

| | |
|---|---|
| **Drug** | Benzhexol HCL |
| **Polymer** | HPMC E5, HPMC 15 |
| **Plasticizer** | PEG400, Glycerol |
| **Surfactant** | Sodium Lauryl Sulphate (SLS) |
| **Flavouring agent** | vanilla |
| **Sweeting Agent** | Sodium saccharin |
| **Solvent** | Ethanol, water. |

*Drug excipients compatibility :*

*FTIR:* - The FTIR spectra of the benzhexol HCL API and the other excipient that was utilized in the MDFs was noted. The KBr technique used to analyse the material using FTIR spectroscopy. Dried KBr is mixed in an equal amount with approx. 10 mg of a formulation. A mortar and pestle are used to thoroughly mix the material. After that, the powder was scanned at various frequencies. As seen in Figure 3.

Table-2. Formulation Layout in accordance with DOE

| Batch code | HPMC E5 | PEG 400 |
|---|---|---|
| F1 | 50 | 5 |
| F2 | 52 | 12 |
| F3 | 45 | 10 |
| F4 | 40 | 8 |
| F5 | 50 | 5 |
| F6 | 40 | 7 |
| F7 | 45 | 4 |
| F8 | 53 | 20 |
| F9 | 42 | 6 |

*Mouth dissolving film evaluation parameter:*

*Morphological Properties :* Typically, homogeneity, colour, transparency, and Odor have been evaluated for MDFs. The whole mixture is kept at the room temperature[20].

*Film thickness :* A micrometre screw gauge, with a 0–10 mm range and a 0.001 mm rotation, was used to measure the film's thickness. Three separate estimates were made[1,8,9].

*In - Vitro disintegration test :* There are several approaches that have been allowed for the disintegration test. place 10 millilitres of distilled water in a beaker together with the necessary-sized film (2 cm in diameter. The point at which the film began to disintegrate or melt was called the disintegration time. Every research was carried out in duplicate for each batch[7,14].

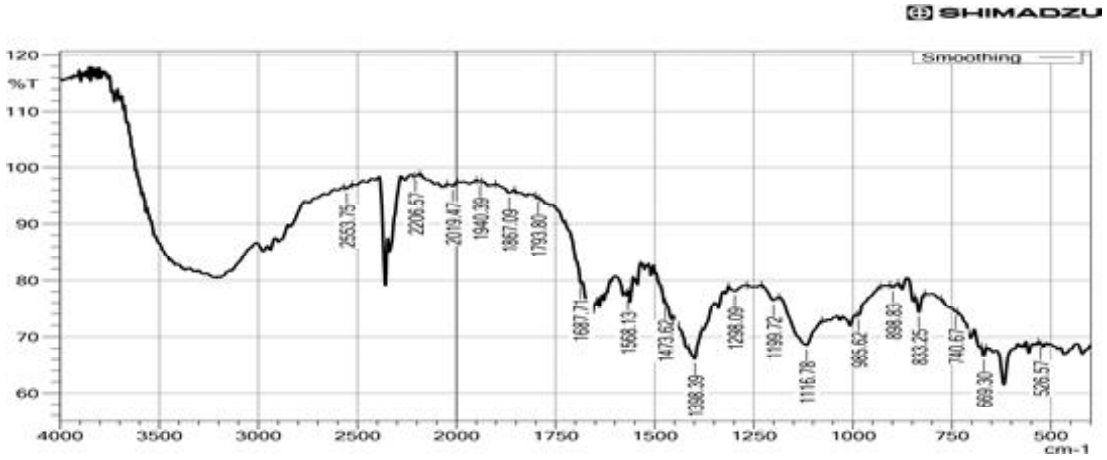



Fig. 3. FTIR spectra of Drug- Excipient

pH *value :* The film was dissolved in 10 millilitres of clean water to determine the pH [22]. After allowing the formulation's surface to come into touch with the electrode of the pH meter for one minute to settle in, the pH was measured[3]. Each calculation was repeated three times. The film must have a pH that is almost constant.

*Folding endurance :*

Folding endurance testing is required for understanding the film's flexibility during handling and storage. To test a film's folding endurance, it was folded in the same place repeatedly until it broke. Consideration is given to good film qualities. A two-centimetre piece of film was consistently cut, then folded in the same spot many times until it broke down. Every determination was made three times[12,17,21].

*Percentage elongation :*

When tension is applied to the film during testing, it stretches and is considered to be in strain. In general, As the concentration of plasticizer increases, the film elongates. The length of the film (%) calculated.

*Drug content :* To determine the amount of drugs solutions containing 20 µg/ml were obtained by dissolving a 4 cm2 film in 100 ml of water. After extracting a 2 ml sample, 10 ml of water was used to dilute it. After that, the solution was examined using a UV Spectrophotometer set to the drug's ʎ max after being filtered via Whatman filter paper. Content uniformity tests were performed in duplicate for each batch of the film[8,15]. Results are described in Table-6 and Graph1.

*In-vitro dissolution studies :*

Pharmacological experiments on Benzhexol HCL Mouth Dissolving Films were conducted using Franz Diffusion Cell Apparatus, measuring 3 cm in diameter on exterior, 2.8 cm on the inside, 8 cm in height, and 30 ml in capacity. The receptor compartment

was constantly stirred at 100 rpm while it was maintained at 37°C. A 1 ml sample was taken at a Replace with an equal volume of the dissolving liquid that has been equilibrated at the same temperature during a predetermined 30-minute period. With the drug's ʌ max set on a UV Spectrophotometer, the drug concentration in the extracted sample was determined. Every study was conducted in triplicate, with the film sink conditions being maintained for every batch[3].

*Drug characteristics :*

*Physical appearance :* The colour, Odor, character, and solubility of benzhexol HCL were visually evaluated. This table summarizes the results: Table-3

Table-3. Physical Appearance

| Serial No. | Physico-chemical | Benzhexol HCL Properties |
|---|---|---|
| I | Colour | White |
| II | Odor | Odourless |
| III | Nature | Amorphous |
| IV | Solubility | Ethanol & Water |

**Melting Point of Drug**: - It was discovered that benzhexol HCL has a melting point of 115°C

Table-4. Benzhexol HCL Melting Point

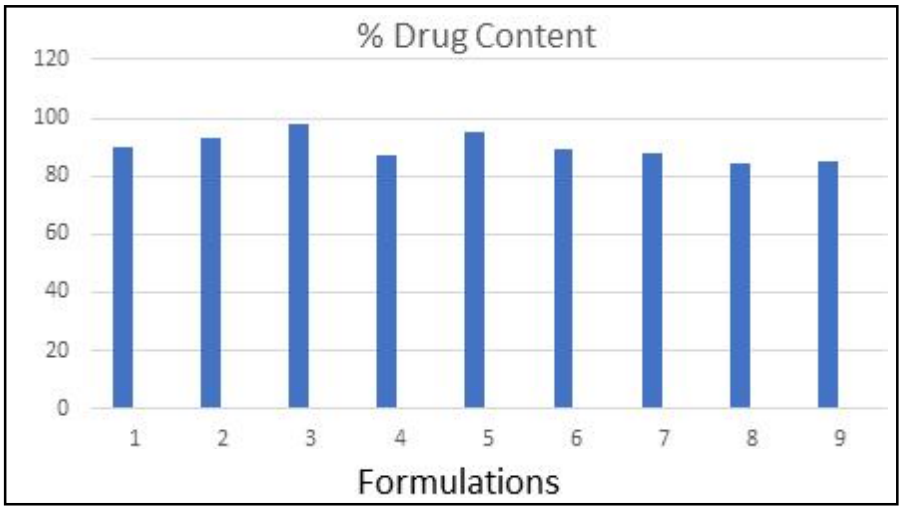
| Serial No | Melting Point | Mean | Theoretical Melting Point |
|---|---|---|---|
| 1 | 111° | | |
| 2 | 114° | 114°C | 114°C-115°C |
| 3 | 115 | | |

Table-5. Evaluation Parameter of Mouth Dissolving Film:

| Batches | Film Thickness | PH | Percentage Elongation | Folding Endurance | Disintegra-tion Time | Drug Release |
|---|---|---|---|---|---|---|
| F1 | 0.15 | 6.15 | 1.45 | 70 | 10 | 87 |
| F2 | 0.13 | 6.65 | 2.0 | 62 | 15 | 92 |
| F3 | 0.10 | 6.70 | 1.65 | 74 | 17 | 96 |
| F4 | 0.15 | 6.44 | 2.78 | 86 | 16 | 91 |
| F5 | 0.17 | 6.30 | 2.55 | 81 | 25 | 94 |
| F6 | 0.16 | 6.55 | 1.88 | 79 | 21 | 87 |
| F7 | 0.18 | 6.87 | 2.46 | 90 | 24 | 88 |
| F8 | 0.14 | 6.75 | 1.22 | 87 | 19 | 83 |
| F9 | 0.17 | 6.55 | 2.78 | 73 | 17 | 88 |

Table-6. Drug Content

| F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|
| 89 | 93 | 98 | 87 | 95 | 89 | 88 | 84 | 85 |



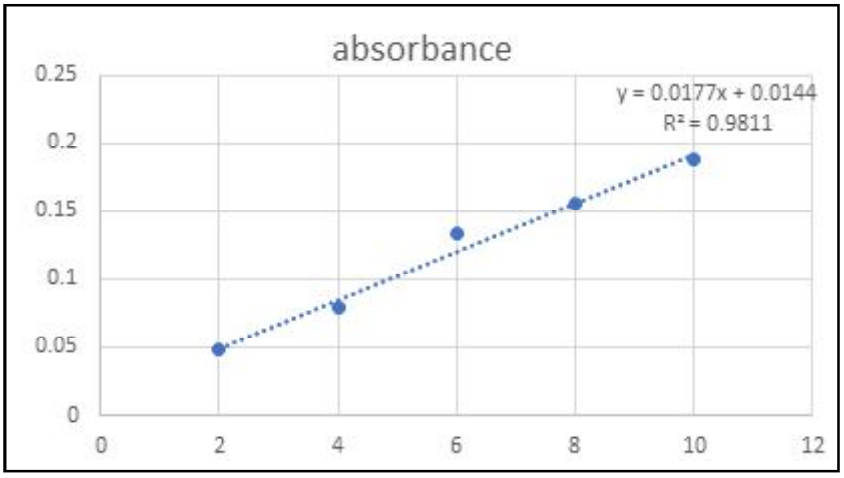

Graph 1. - % of Drug content

*Drug calibration curve :*

A UV spectrophotometer (Shimadzu UV 1700) was used to determine the benzhexol HCL standard curve in distilled water. The absorbance at 222 nm was measured and is displayed in Table-7. The absorbance vs. concentration standard plot is displayed in Graph 2.

Table-7. UV Spectroscopy Results at Different concentration

| Concentration (µg/ml) | Absorbance at 222 nm |
|---|---|
| 2 | 0.048 |
| 4 | 0.079 |
| 6 | 0.134 |
| 8 | 0.155 |
| 10 | 0.187 |




Graph. 2. Calibration curve of Benzhexol HCL

*Stability studies :*

Stability tests for Benzhexol HCL were conducted in a stability chamber. The following results were derived from stability studies performed for one month at 40°c and 75% relative humidity. The optimized film showed no significant differences in terms of weight loss, disintegration time, percentage of medication content, or appearance after storage. The results indicate that formulations containing Benzhexol HCL are stable and maintain their original qualities. (Graph-2).

*Result of the optimized Batch F7 stability study :*

Table-8.

| Sr No | Parameter | 1st week | 3rd week | 6th week |
|---|---|---|---|---|
| 1. | Thickness | 0.18 | 0.18 | 0.18 |
| 2. | PH | 6.87 | 6.87 | 6.87 |
| 3. | Disintegration | 28 | 28 | 28 |
| 4. | Folding endurance | 90 | 90 | 90 |
| 5. | Percent elongation | 2.46 | 2.40 | 2.40 |

The purpose of this study was to produce a mouth-dispersing film containing benzhexol HCL to facilitate rapid medication release and manage children's chronic drooling. In order to improve patient compliance and bioavailability for increased therapeutic efficacy, this work demonstrates that Benzhexol HCL mouth dissolving films can be made Through FT-IR studies, the compatibility of benzhexol HCL with polymers was confirmed. The plasticizer PEG 400 is combined with the film-forming polymer HPMC E5. The bitter taste of the medication is efficiently covered up by the sweetener sodium saccharin.

As polymer concentration increased the films' tensile strength, percentage elongation, and folding endurance improved due to their elasticity. The time required for the film's disintegration and mouth dissolving increased with the polymer concentration because more fluid was needed to Wet the film within your mouth. Studies on content uniformity show that the drug is dispersed equally across the entire film. According to the current study's findings, the formulated films have adequate film parameters. The solvent casting method can be used to create mouth dissolving films containing benzhexol HCL, it can be concluded. Additionally, it may be a unique medicinal dosage form intended for paediatric use.

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