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Research Article

Formulation Development and Evaluation of Clotrimazole Buccal Tablets

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ABSTRACT

The current study's objective is to develop and assess the Clotrimazole Buccal Tablets. Clotrimazole buccal tablets are made with locust bean gum, Methocel K4M, and Methocel K15M. A buccal medication is administered between the gums and the cheek's inner lining. We refer to this region as the buccal pouch. When a medication needs to start working right away or is intended for a child, especially one who is unconscious, it is typically administered in the buccal region. Buccal tablets' benefits include: First pass: Because the liver is avoided, medications have a better bioavailability. Fast absorption: The absorption area is typically rather quick due to the healthy blood supply, particularly for fat-soluble medications. Drug stability-the pH in the oral cavity is relatively neutral.

INTRODUCTION

When medications are administered or stored in the buccal region (the cheek), they diffuse through the oral mucosa (the tissues lining the mouth) and enter the bloodstream directly. This is known as buccal administration. Because buccal administration circumvents first-pass metabolism by avoiding the digestive tract, it may offer some medications greater bioavailability and a quicker onset of action than oral administration. Thin films and tablets are two drug formulations that are administered buccally. Commercially available in buccal forms were the following medications: nicotine as a smoking cessation aid; the opioid drugs buprenorphine, naloxone, and fentanyl; the cardiovascular drug nitroglycerin; the hormone replacement therapy testosterone; the nausea medication prochlorperazine; and the psychiatric drug asenapine [1] an anticonvulsant, used to treat acute epileptic seizures.[2]

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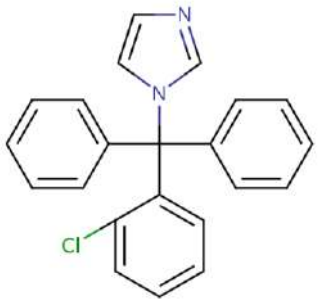

Fig No: 01 Structure of Clotrimazole

METHODOLOGY

Preformulation Studies:

Pre-formulation studies are meant to provide formulators with knowledge that will help them create stable and bioavailable dosage forms. Using pre-formulation parameters increases the likelihood of creating a product that is stable, safe, effective, and acceptable. It also serves as a foundation for improving the drug product's quality [6,7].

Solubility Profile of Clotrimazole

The formulation and efficacy of the antifungal drug clotrimazole can be affected by certain solubility properties. Because of its weak water solubility, clotrimazole may not be as bioavailable when taken orally. It dissolves better in organic solvents such as methanol, ethanol, and chloroform. Clotrimazole's solubility may change with pH; it dissolves better in acidic settings than in neutral or alkaline ones.

pH 6.8 Phosphate Buffer Preparation:

Weighted 11.45 gm of potassium Dihydrogen phosphate and 28.80 gm of disodium hydrogen phosphate and made up to 1000 ml with distilled water.

Calibration Curve of Clotrimazole:

Calibration curve for clotrimazole involves preparing a series of standard solutions of known concentrations and measuring their absorbance using a suitable analytical technique, typically UV-Vis spectrophotometry. Following a step-by-step guide as: After measuring 100 mg of Clotrimazole, it was placed into a 100 ml volumetric flask and dissolved in a pH 6.8 phosphate buffer solution. The volume was then adjusted to 100 ml to achieve a concentration of 1000 µg/ml. From this solution, 10 ml was taken and further diluted to 100 ml with pH 6.8 phosphate buffer solution, resulting in a concentration of 100 µg/ml. From this standard stock solution, aliquots of 0.2 ml, 0.4 ml, 0.6 ml, 0.8 ml, and 1 ml were taken and diluted with pH 6.5 phosphate buffer solution to obtain concentrations of 2, 4, 6, 8, and 10 µg/ml. The absorbance of these solutions was measured at 255 nm against a blank of pH 6.8 phosphate buffer solution.

Compatibility Studies of Drug & Excipients

FTIR can help determine if there is any significant interaction between clotrimazole and excipients used in buccal tablets, such as polymers (e.g., hydroxypropyl methylcellulose, micro crystalline cellulose), fillers, or stabilizers. Changes in peak positions or intensities compared to the pure drug spectra could indicate interactions.

Characteristic Peaks of Clotrimazole:

C–Cl stretching**:** Clotrimazole contains a chlorinated aromatic ring, showing peaks in the range of 600-800 cm^{-1}. C=N stretching (imidazole ring): Clotrimazole has an imidazole ring, which shows a characteristic peak around 1600-1700 cm^{-1}. Aromatic C–H bending**:** Peaks typically appear in the region of 1450-1600 cm^{-1}. Aromatic C=C stretching**:** Peaks in the range of 1500-1600 cm^{-1} may be observed. The region between 600-1500 cm^{-1} serves as the fingerprint region, unique to clotrimazole, and helps confirm its presence. Deviations here might indicate formulation issues or degradation. Shifts in peaks, such as broadening or intensity changes in the O–H or N–H regions (if present due to excipients or moisture), may suggest hydrogen bonding. This can provide insights into the drug release profile and stability in the buccal environment.

Method of Formulation of Clotrimazole Buccal Tablet:

Manufacturing clotrimazole buccal tablets involves formulating the active ingredient, clotrimazole, with specific excipients to create a tablet that adheres to the buccal mucosa for prolonged drug release. This method improves the local therapeutic effect, especially for oral fungal infections. Below is a step-by-step outline of a typical manufacturing method

Formulation of Clotrimazole Buccal Tablets:

Bioadhesive Polymers carrageenan, Locust bean gum, were selected to act as thickening agent or Emulsifier**.** Microcrystalline cellulose used with the Bio Polymers to improve tablet structure which can act as good suspending agent. Xanthum Gum is selected to add to the bulk mixture which act as a binder. Magnesium stearate, talc added to aid in tablet ejection from the mould. The clotrimazole and selected excipients were weighed accurately. The active ingredient and excipients got mixed uniformly using a blender or V-blender to ensure even distribution. Proper mixing is crucial to ensure consistent drug release from each tablet. The formulation can be done in two ways by using wet granulation method and direct compression method. In wet granulation process, If clotrimazole and excipients require binding for a more cohesive mix, wet granulation can be employed using a binding solution which is made with binder mixed with methanol or water. Mix until the powder becomes uniformly wet and forms a dough-like consistency then pass it through the sieve number 16. The obtained granules were dried in an oven or fluidized bed dryer ensuring the granules are free-flowing and stable. The dried granules through a screened to achieve uniform granule size. Add lubricants magnesium stearate and talc. Mix lightly to avoid breaking the granules. Then they got compressed using tableting tool. In the second method which is direct compression method, If the powder blend flows well, it can be directly compressed into tablets without granulation.

RESULTS AND DISCUSSIONS:

Pre formulation Studies:

Solubility Profile of Clotrimazole

Solubility studies were carried out to select a suitable solvent to dissolve the drug and to select the dissolution medium.

Table1: Solubility studies

Solvent	Solubility
Water	practically insoluble
PhosphatebufferpH6.8	Soluble
Ethanol	Soluble
Methanol	Soluble

Development of Calibration Curve of Clotrimazole:

In the validation studies, it was found that the estimation of Clotrimazole by spectrophotometric method at 255 nm has good reproducibility, at the concentration between 2-10 µg/ml. Correlation between concentration and absorbance was found to be 0.9976 which is closer to 1.

Table. 2 Calibration curve of Clotrimazole

Concentration(µg/ml)	Absorbance
0	0
2	0.125
4	0.267
6	0.367
8	0.476
10	0.581
12	0.701

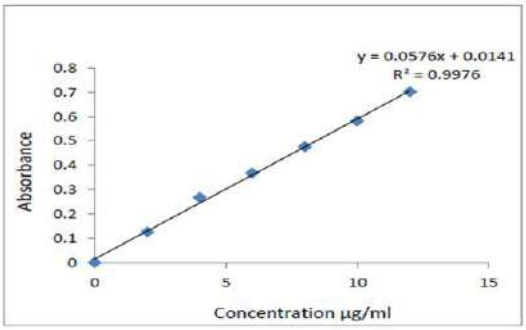

Fig. 2 Calibration curve of Clotrimazole

Compatibility Studies of Drug & Excipients

In the present study, physical mixture of Clotrimazole solid form along with different polymers were prepared and analyzed by FTIR to find out the compatibility between the drug and polymers. The IR spectra of Clotrimazole along with the physical mixture of Clotrimazole with different polymers are shown from the graph which showed that the drug and excipients.

Table. 3 FTIR interpretation of Drug Clotrimazole

FTIR Interpretation of Drug Clotrimazole				
Samples	**Functional group**	**Type of vibration**	**Characteristic absorption (cm^{-1})**	**Test absorption (cm^{-1})**
Clotrimazole	C-H(Aromatic)	Stretching	2900-3050	3042.67
	C-H (Aliphatic)	Bending	1350-1480	1443.87
	NH	stretching	3400-3500	3429.78
	C=C	Stretching	1400-1600	1455.98
	C-Cl	Stretching	650-750	745.85
	C=N	Stretching	1550-1580	1562.95
	C-N	Stretching	1200-1300	1287.95

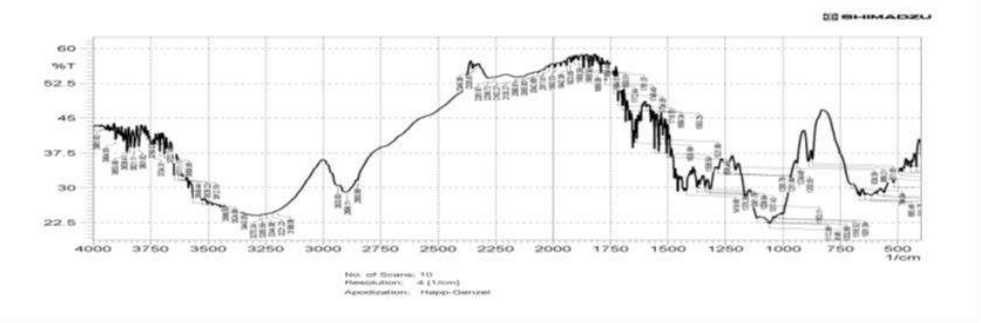

Fig 3. FTIR of Clotrimazole

Formulation of Clotrimazole buccal Tablets:

The clotrimazole and selected excipients were weighed accurately. The active ingredient and excipients got mixed uniformly using a blender or V-blender to ensure even distribution. Proper mixing is crucial to ensure consistent drug release from each tablet. wet granulation can be employed using a binding solution which is made with binder mixed with methanol or water. Mix until the powder becomes uniformly wet and forms a dough-like consistency then pass it through the sieve number 16. The obtained granules were dried in an oven or fluidized bed dryer ensuring the granules are free-flowing and stable. The dried granules through a screened to achieve uniform granule size. Add lubricants magnesium stearate and talc. Mix lightly to avoid breaking the granules. Then they got compressed using tableting tool. Using this method 9 different preparations were done by named CZL1, CZL2, CZL3, CZL4, CZL5, CZL6, CZL7, CZL8, CZL 9 using different proportions of excipients as shown in the below table.

Table 4: Formulation of Clotrimazole buccal Tablets

Formulation No.	Clotrimazole	Xanthan gum	Carageenan gum	Locust Bean Gum	Mag. Stearate	Talc	MCC pH 102
CZL1	10	10	-	-	3	3	QS
CZL2	10	20	-	-	3	3	QS
CZL3	10	30	-	-	3	3	QS
CZL4	10	-	10	-	3	3	QS
CZL5	10	-	20	-	3	3	QS
CZL6	10	-	30	-	3	3	QS
CZL7	10	-	-	10	3	3	QS
CZL8	10	-	-	20	3	3	QS
CZL9	10	-	-	30	3	3	QS

CHARACTERIZATION OF CLOTRIMAZOLE BUCCAL TABLETS

Physical characters of formulated Buccal Tablets:

Thickness of all formulations were found uniform and ranged from 2.5mm to 3 mm

Drug Content

Drug content in each formulation ranging from CZL1, CZL2, CZL3, CZL4, CZL5, CZL6, CZL7, CZL8, CZL 9 analysed spectrophotometrically, and it was noted that all the formulations shown a satisfactory drug content values ranging from 89 – 99% release of the drug from formulation prepared.

Weight Uniformity:

From each batch, five tablets were taken on a digital balance to weight and observed that weight of the entire formulated sample in each formulation was uniform.

Hardness: this refers to the tablet's mechanical strength, which affects its ability to withstand handling and storage. The formulation attains a hardness range from 3.8 kgf (kilogram force) which the test was done with Monsanto hardness tester.

Friability: Friability measures the tablet's tendency to chip or crumble, ensuring durability. This test done using a friabilator where tablets are rotated and subjected to abrasion. The formulations shown the weight loss less than 1% which is in the limit.

Surface pH:

This Ensures the tablet's pH is compatible with the buccal mucosa to minimize irritation. The formulations were ideally close to neutral within the range of pH 6.8–7 to prevent mucosal irritation This was tested by slightly wetting the tablet with water and using a pH meter probe.

Mucoadhesion Strength:

This assesses the tablet's ability to adhere to the buccal mucosa, which is critical for prolonged retention. This was tested by using a texture analyzer or tensile tester to quantify the force needed to detach the tablet from a mucosal substrate which given the range within the limit.

Swelling Index:

This measures the tablet's capacity to swell upon contact with moisture, which affects drug release and adhesion. Tablets are weighed initially and placed in simulated saliva solution, then weighed periodically. The swelling index is calculated based on the increase in weight which given the range 65-70% which got fallen in limited range usually 10-80% within a specified time frame (usually 1–6 hours).

In Vitro Drug Release Profile:

This ensures the release of clotrimazole for therapeutic efficacy over an extended period. Tablets are subjected to dissolution testing in the simulated medium, and drug release is measured over time using a UV spectrophotometer or HPLC.

CONCLUSION:

The goal of the current examination was to create buccal detailing of Clotrimazole to maintain consistent remedial degrees of the medication for more than 12 hours. "From the disintegration considerations, it was evident that the definition (CZL8)" demonstrated better and desired medication discharge example, i.e., 97.08 % "in 12 hours." It aimed for an energy system with 0% request discharge. Bypassing the liver and digestive system, buccal pills enter the bloodstream straight through the oral mucosa. Higher bioavailability and more consistent drug levels result from avoiding first-pass metabolism, which can degrade a significant amount of some medications when given orally. Compared to oral tablets that need to transit through the digestive system, these formulations may have a quicker beginning of action. This can be particularly helpful for medications used to treat acute symptoms like nausea and discomfort. Because buccal tablets are simple to use and don't require water, they're perfect for patients who have trouble swallowing, such as young children or elderly people. Furthermore, some buccal pills are made to dissolve gradually, requiring fewer dosages to provide prolonged relief. Bypassing the stomach and intestines, these buccal tablets might lessen the frequent gastrointestinal adverse effects of oral tablets, like nausea and stomach irritation. They offer a more stable environment for medications that are susceptible to stomach acid or digestive system enzymes, which makes them perfect for delivering certain proteins, peptides, and hormones.

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