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# FORMULATION AND DEVELOPMENT OF BIOADHESIVE FILM OF ONDANSETRON HYDROCHLORIDE USING OKRA POLYMER

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***Abstract:*** Difficulty or incapability in swallowing pills/pills throughout or after chemotherapy in addition to unconscious patient. Bioadhesive film of ondansetron hydrochloride have been organized for the prevention and remedy of chemotherapy-precipitated emesis in addition to in films of varying polymeric composition have been prepared if you want to facilitate initial as well as prolonged drug launch that could take care of acute as well as delayed emesis. Bioadhesive films were prepared the usage of polymers which include okra, hydroxypropyl methyl cellulose (HPMC K15M), polyvinyl alcohol (PVA), polyvinyl pyrrolidone (PVP K30), ethyl cellulose, and polyethylene glycol 400 (PEG 400). The impact of awareness of these polymers on physical properties and drug launch were studied. All of the film had been organized by means of solvent casting method. In every other part of the examine, the impact of drug attention on bodily and bioadhesive houses of film have been assessed, preserving the polymer awareness fixed. Film containing okra polymer showed good bioadhesive. Growing the awareness of okra in the film retarded drug release and expanded residence time, but, reduced bioadhesive. At a fixed polymer attention and ratio, films prepared the usage of an extended drug content confirmed an elevated bioadhesive. Film prepared the use of Okra polymer supplied preliminary fast accompanied by way of sustained drug launch over a period of 6 h. Given the promising results, the observe concluded that the evolved buccal film have the ability to release ondansetron required for chemotherapy brought about acute and delayed emesis and additionally beneficial in subconscious patient.

***Key words*** **- Bioadhesive films, Ondansetron hydrochloride, Okra polymer, HPMC K15M, Polyvinyl alcohol (PVA), Polyvinyl pyrrolidone (PVP K30), Ethyl cellulose Etc.**

## 1. INTRODUCTION

Chemotherapy drugs can directly stimulate the CTZ, a specialized area in the brain that detects toxins and initiates the vomiting reflex. This stimulation can result in feelings of nausea and vomiting [1]

Ondansetron hydrochloride, a 5HT3 antagonist, is an efficacious antiemetic medication used to treat nausea and vomiting caused by cancer chemotherapy. Due to first pass metabolism, it has a relatively short half-life of three to five hours and only indicates 60 to 70% of oral bioavailability[2]

Buccal drug delivery is a particularly efficient method for increasing bioavailability. This is due to the buccal mucosa's richest blood supply, which allows drug molecules immediately passage into the systemic circulation.[3, 4]

Buccal drug delivery overcome hepatic first pass metabolism. Bioadhesive films are tiny, paper-thin.[5]

The oral buccal route is a specialised form of oral drug delivery where medications are administered through the buccal mucosa, which is lining of the inner cheek and floor of the mouth[6]. Instead of swallowing medication, it is held in the mouth or against the cheek to allow for absorption through the buccal mucosa and direct entry into the bloodstream.[7] This route offers several advantages; Rapid absorption, avoidance of gastrointestinal issues, enhanced bioavailability, patient convenience and compliance, control drug release.[8]

Bioadhesive polymers or bioadhesive materials are a class of polymers is that have the ability to adhere to biological tissue. Bioadhesive polymers can be natural or synthetic in origin. Natural polymers are biocompatible and biodegradable. Bioadhesive polymers can be formulated in different forms, including gels, films, nanoparticles, and hydrogels. The bioadhesive films are prepared by the casting method, where a polymer-drug solution is spread or poured on a suitable substrate and dried to form a thin film[9, 10]
Okra, or Abelmoschus L., is a dicotyledonous crop that is self-pollinating and a part of the Malvaceae family and plantae kingdom.[11] Okra polymer contains chemical constituents like, D-galactose, L-rhamnose and L- galacturonic acid.[12] Okra mucilage is known for its ability to create a sustained release matrix.[13] The purpose of the research work is to assess the ondansetron hydrochloride release from a film composed of an okra polymer.

## 2. MATERIALS AND METHODS:

### 2.1 Materials

Hibiscus esculentus fruits were brought from the local market. Ondansetron hydrochloride was procured from Neon laboratory, India. The hydroxypropyl methyl cellulose (HPMC K15M), polyvinyl alcohol (PVA), polyvinyl pyrrolidone (PVP K30), ethyl cellulose, and polyethylene glycol 400 (PEG 400) were procured from Loba Chemie Pvt. Ltd., India.

### 2.2 Extraction of polymer from okra fruit:

Okra was collected from the local market. Wash and clean the okra. Cut the pods into small pieces and remove the seeds. Okra was boiled for 4 hours and soaked in water. Kept aside for 2 hours and squeezed into a muslin bag. Equal volumes of ethyl alcohol were added to the filtrate. Separated the mucilage and dried in oven at 45℃. The obtained powder was passed through #80 and stored in a desiccator.[13]

### 2.3 Preparation of backing layer[14]

The process of solvent casting was used to prepare the backing layers. A solution of EC (5%w/v) was created by dissolving it in a mixture of acetone and isopropyl alcohol in a ratio of 65:35. To enhance flexibility, dibutyl phthalate were added as a plasticizer. The plasticized Ethyl cellulose solution was then poured onto a level surface in a petri plate. The petri plate was covered with an inverted funnel.

### 2.4 Preparation of bioadhesive buccal film:[15, 16]

The solvent casting method was used to create films. The polymers were dissolved in their respective solvents. This polymeric dispersion was stirred on a magnetic stirrer for one hour to obtain a uniform and clear solution. Polyethylene glycol was added as a plasticizer and stirred for 30 minutes. The drug solution was added to the polymeric mixture and sonicated for 15 minutes. Kept aside for a few hours. This solution was poured onto a backing layer and dried overnight.

**Table: Formulation Batches**

| Ingredients (mg) | F1 | F2 | F3 | F4 | F5 |
|---|---|---|---|---|---|
| Ondansetron Hcl | 79.13 | 79.13 | 79.13 | 79.13 | 79.13 |
| HPMC E15 | 360 | 300 | 180 | 60 | - |
| PVP K30 | 75 | 75 | 75 | 75 | 75 |
| PVA | 150 | 150 | 150 | 150 | 150 |
| Okra polymer | - | 60 | 180 | 300 | 360 |
| PEG 400 (ml) | 2 | 2 | 2 | 2 | 2 |
| Distilled water (ml) | 30 | 30 | 30 | 30 | 30 |

## 3.EVALUATION OF BIO ADHESIVE BUCCAL FILM:

### 3.1 Pharmaceutical parameters:

#### 3.1.1 Thickness of film:

The film's thickness was measured at six different locations on films from each batch using a Vernier caliper, and average value was calculated.[17, 18]

#### 3.1.1 Weight uniformity

The weight uniformity of films was examined by weighing six randomly chosen films from each batch using an electronic balance.[19, 20]

#### 3.1.2 Folding endurance

This test is conducted to assess the film's tensile strength. It involves repetitively folding the film at a specific point until it breaks.[21]

#### 3.1.3 Swelling index

Swelling of the film was measured by placing the film on the surface of an agar plate and keeping it in an incubator maintained at 37℃. The weight of the swollen film was determined after 2 hours.[22] the percentage of swelling was calculated using equation:

$$\% S = Wt - W_0 / W_0 \times 100$$

Where,

Wt = weight of swollen film after time t

$W_0$ = initial weight of film at t = 0

### 3.2 Mechanical properties:

#### 3.2.1 Mucoadhesive strength

This study was done on physical balance. Porcine buccal mucosa was turned outward and wet with a few drops of PBS (pH 6.8) to help it adhere to a dry petri dish surface. A glass vial with a buccal film of 2cm in diameter and adhesive was used to replace the balances's right side pan, maintaining enough weight on the left pan to allow the balance to be adjusted for equal oscillation. A 5g weight was taken off the left side, causing the pan to tilt downwards. Then the buccal film was placed on moistened mucosa and left in contact for a duration of five minutes. Then weights were gradually raised on the left pan until the attachment failed. [23, 24]

### 3.3 Biocompatibility studies:

#### 3.3.1 Surface pH:

The irritation potential of a film on mucosal membranes was assessed by measuring its surface pH. The film was applied to a solidified agar medium, which was kept at 37℃ in an incubator for 2 hours. The pH of the swollen film was then determined using pH meter.[25]

### 3.4 Physicochemical characteristics:

#### 3.4.1 Differential scanning calorimeter (DSC)

The thermal characteristics of the formulation batches were analysed utilising a different scanning calorimetry. The sample underwent heating within a specific temperature range for evaluation. This can be evaluated by gradually increasing temperature of the sample in an aluminium pan from its initial room temperature to a higher temperature.[23]

#### 3.4.2 Scanning Electron Microscopy (SEM)

SEM analysis was conducted using a SEM instrument. A portion of the film was affixed to the sample holder using double sided adhesive tape. The film on the SEM grid was then left to dry in the air, and images were captured at various levels of magnification.[21, 22]

### 3.5 Characterization of film

#### 3.5.1 Drug content uniformity

Content uniformity is determined by a 2-cm film (without a backing layer) was dissolved in 10 ml of PBS (pH 6.8). The resultant solution was filter using whatman filter paper, and the amount of Ondansetron hydrochloride was calculated using a spectrophotometric method of a wavelength of 248 nm (Shimadzu UV 1900i). The averages of three conclusions were obtained. [22]

#### 3.5.1 In vitro drug release study

The in vitro dissolution test was carried out on a basket dissolution apparatus. Samples of ondansetron films were exactly weighed. 900ml of PBS (pH 6.8) at 37℃ ± 5℃ was used as the dissolution medium with stirring rate 500 rpm.A film of 2×2cm (4cm$^2$) was kept in basket. During the study, 10ml of sample were withdrawn at 15, 30, 45, 60, 75, 90, 105 and 120 min and replaced by fresh buffer. The samples were filtered using muslin cloth and used for UV determination at 248nm. [23]

#### 3.5.2 Ex-vivo permeation study

A modified Franz glass diffusion cell was used to determine the ex vivo buccal permeation of ondansetron hydrochloride through the porcine buccal mucosa. The buccal mucosa of a goat was obtained from a nearby slaughterhouse and used within 2 hours. The film was applied to the smooth mucous membrane surface, and subsequently, the donor and receptor compartments were clamped in close proximity. Freshly obtained porcine buccal mucosa was inserted between these donor and receptor compartments. The receptor compartment was filled to touch the membrane with PBS (pH 6.8). The entire setup was kept at a temperature of 37℃, and the liquid in the system was stirred at a speed of 50 rpm.At appropriate time intervals, a 2 ml sample was taken out and replaced with an equal amount of medium at regular intervals, followed by spectrophotometric analysis at 248 nm.[24, 25]

## 4. RESULT AND DISCUSSION

### 4.1 Pharmaceutical parameters

#### 4.1.1 Weight variation and Thickness of film

The weight variation ranged from 0.55 ± 0.010 to 0.085 ± 0.018 mg, and thickness was obtained in the range between 0.016 ± 0.05 to 0.02 ± 0.005 mg.

#### 4.1.2 Folding endurance

All films formulated were smooth and of good flexibility. The folding endurance obtained upto 412 folds.

#### 4.1.3 Swelling index

The extent of swelling in the film impacts both its ability to adhere to biological surfaces and the pattern of drug release. The swelling index was observed at up to 90%.

### 4.2 Mechanical properties:

#### 4.2.1 Mucoadhesive strength

The relationship between swelling index and mucoadhesive strength is such that when the swelling index increases, the mucoadhesive strength also increases. A direct correlation was observed between the concentration of OP in the film and the force needed for detachment, indicating that the higher concentration of OP resulted in an increased force required to separate the film. The mucoadhesive strength varied from 16.67 to 19.62 N.

### 4.3 Biocompatibility study:

#### 4.3.1 Surface pH

The films were found to have a pH range of 6.28 - 6.5, which is in proximity to the pH of saliva. This indicates that the films could be potentially mild and non-irritating to the mucosal membrane.

**Table 1: Evaluation parameter**

| Formulation batch | Weight (mg) Mean ± SD | Thickness (mm) | Folding endurance | Swelling index (%) | Mucoadhesive strength (N) | Surface pH | Drug content (%) |
|---|---|---|---|---|---|---|---|
| **F1** | 0.15± 0.021 | 0.2 ± 0.1 | 375 | 68 | 16.67 | 6.28 ± 0.35 | 97.38 |
| **F2** | 0.06± 0.008 | 0.16 ± 0.05 | 397 | 73 | 17.16 | 6.45 ± 0.32 | 95.18 |
| **F3** | 0.085±0.018 | 0.2 ± 0.005 | 402 | 83.33 | 19.12 | 6.5 ± 0.34 | 93.77 |
| **F4** | 0.083 ± 0.015 | 0.16 ± 0.011 | 409 | 87.21 | 18.14 | 6.35 ± 0.28 | 95.58 |
| **F5** | 0.055 ± 0.010 | 0.2 ± 0.1 | 412 | 90 | 19.62 | 6.5 ± 0.25 | 96.38 |

### 4.4 Physicochemical characteristics:

#### 4.4.1 Differential Scanning Calorimetry (DSC):

The thermal stability of the drug and additives was assessed using DSC (Differential Scanning Calorimetry), which yielded valuable insights.

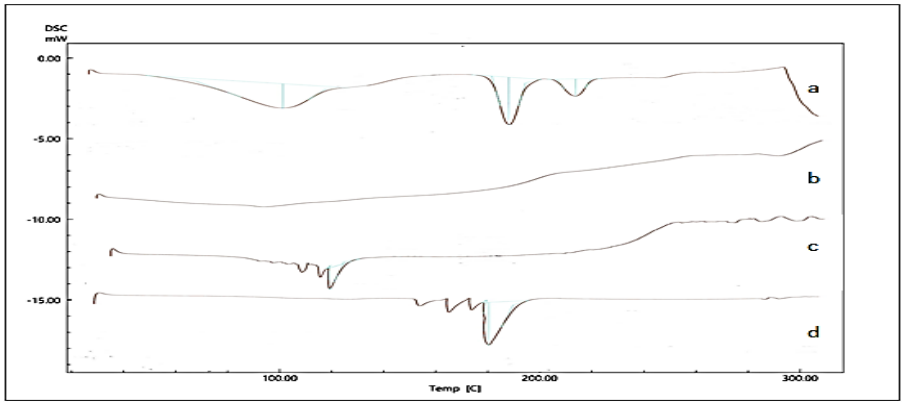



**Figure 1:** DSC thermogram of (a) Ondansetron hydrochloride (b) Okra polymer (c) Okra placebo (d) Formulation batch F5

The thermogram of the drug showed a clear endothermic peak at 187.80℃, which represented the melting point of ondansetron hydrochloride. The temperatures at which the melting process begins and ends for ondansetron hydrochloride is 181.52 ℃ and 193.81℃. At a temperature of 104.42℃, there is a significant endothermic process (Salem et al., 2001). Figure 1(b) revealed a prominent peak at 120℃, signifying the detection of bound moisture within okra gum (Zaharuddin et al., 2014). Figure 1 (c) The thermogram shows the endothermic peak at 157.38℃. The DSC of formulation batch F5 (figure 1. (d) ) shows an endothermic peak at 185.97℃, which is close to the DSC result of ondansetron hydrochloride.

#### 4.4.2 Scanning Electron Microscopy (SEM)

The distribution of particles within the film is not consistent throughout its structure. A magnified image of the film is obtained through a scanning electron microscope, revealing details at a 10,000 kX and 25, 00 kX.

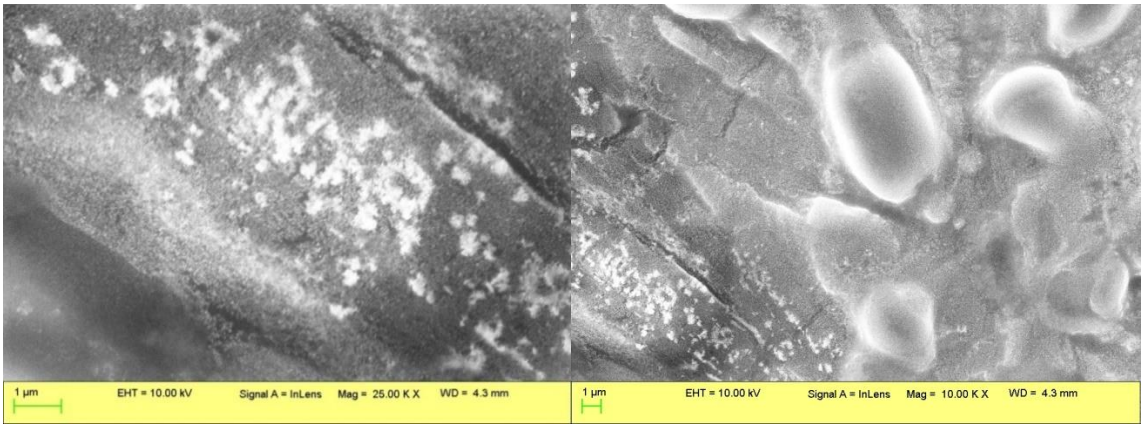



**Figure 2:** Surface morphology of formulation batch F5

### 4.5 Characterization of okra film

#### 4.5.1 Drug content uniformity

The drug content measured during the experiment closely matched the expected value, with a range of 93.77% to 97.38% and showed minimum variation.

#### 4.5.2 In vitro drug release

Formulation batch F5 exhibited the release rate, upto 65.55% within 6 hours during in vitro testing. From the in vitro release study it was concluded that the F5 batch showed the sustained release due to the higher concentration of okra polymer.

#### 4.5.3 Ex vivo permeation study

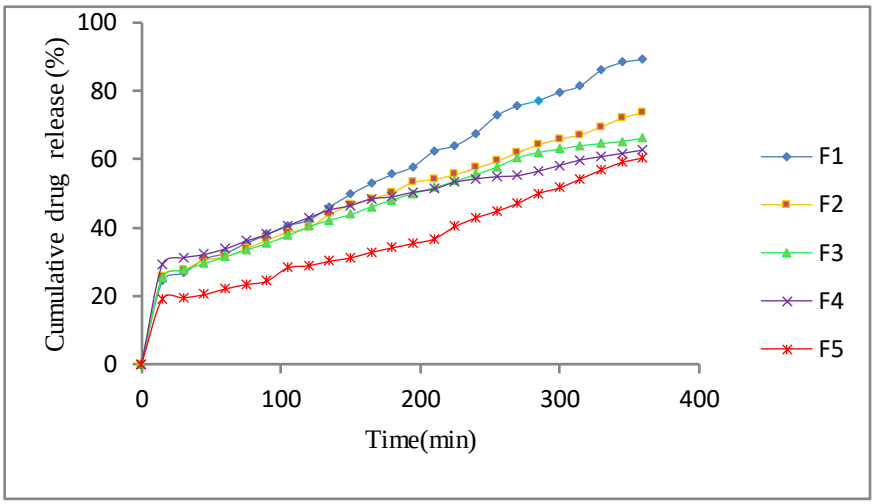
The drug release rate decreased significantly when the concentration of okra polymer increased. It showed the sustained release of drugs from the film. Batch F5 showed drug diffusion 60.37% after 6 hours. The controlled release of the drug from the formulation occurred through a combination of two mechanisms: the rapid hydration and swelling of the polymer, leading to the formation of a gel-like or highly viscous matrix, and swollen matrix, resulting in a gradual and slow release of the drug.

**Figure:** In vitro drug release of buccal film

## 5. CONCLUSION

In conclusion, the utilisation of okra polymer in the development of bioadhesive buccal film holds significant potential for various applications. Bioadhesive buccal films formulated with okra polymer have shown promising results in improving drug delivery efficiency and patient compliance. Incorporating OP into the formulation can enhance the adhesive properties of the buccal

film, leading to a slower release of the drug and enhanced drug absorption. As a result, OPs show potential as beneficial ingredients in adhesive buccal formulations, either individually or in conjugation with other polymers.

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