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"FORMULATION AND EVALUATION OF ORAL FAST DISSOLVING FILMS"

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ABSTRCT:

The present investigation was undertaken with the objective of formulating oral fast dissolving film of the antiemetic drug Domperidone to enhance the convenience and compliance by the elderly and pediatric patients. Domperidone consists antiemetic properties related to its dopamine receptor blocking activity at both the chemoreceptor trigger zone and at the gastric level. Domperidone is a prokinetic & works on the region in the brain that controls vomiting. It is the best option for healing nausea and it is useful for treating vomiting during journeys. Mouth dissolving films were formulated by the solvent casting technique. Films were formulated using Hydroxy Propyl Methylcellulose (HPMC-E5) as a film forming agent, PEG-400 as a plasticizer. The dependent variables were the Percentage Drug Release in 5 minutes and Folding endurance. The thickness, folding endurance, tensile strength, disintegration time, in vitro drug release and drug content uniformity of the prepared films were evaluated. The high percent drug release of the film at pH 6.8 in phosphate buffer suggests its potential application in treating common cold and rhinitis, where there is a requirement of fast drug bioavailability. The overall results suggested that the prepared Domperidone fast dissolving oral films can be used as an attractive and alternative to the commercial available immediate release and conventional tablets resulting improved patient adherence.

KEYWORDS: Oral Fast Dissolving Film, Domperidone, HPMC-E5, Solvent Casting Method.

INTRODUCTION:

The most common method of administration is oral. Oral dosage forms account for between 50 and 60 percent of all dosage forms because to their high patient compliance, ease of swallowing, lack of pain, and adaptability.[1] The oral route is currently the most popular method for drug delivery because it has many advantages over other drug administration routes. However, oral drug delivery systems still require advancements because of certain drawbacks specific to a particular patient class, which includes pediatric, geriatric, and dysphasic patients who have a variety of medical conditions and have difficulty swallowing or chewing solid dosage forms.[2] When placed on the tongue, oral thin films—rectangular polymeric films the size of a postage stamp—instantaneously dissolve and disintegrate.[3] Fast dissolving films are formulated using polymers, active pharmaceutical ingredients (API), plasticizers, saliva stimulating agents, sweeteners, flavors, preservatives and colors. Fast dissolving film is simply placed on the patient's tongue or any oral mucosal tissue, instantly wet by saliva the film rapidly hydrates and adheres onto the site of application.[4] The fast dissolving drug delivery system are specially designed for the drugs which have extensive first pass metabolism and have low dose, for the enhancement of bioavailability.[5] Technology Catalysts forecasts the market for drug products in oral thin film formulations was valued of $500 million in 2007 and could reach $2 billion in 2012. Based on upward global growth trends of the past decade, the fast dissolving dosage market could produce revenues of $13 billion by 2015.[6]

Oral fast dissolving films :

Fast dissolving films are most advance formulation was developed i.e. oral fast dissolving films. form of solid dosage form due to its flexibility. It improve Fast dissolving films (FDF), a type of oral drug efficacy of Active pharmaceutical ingredient (API) delivery system for the oral delivery of the drug, was dissolving in the short duration oral cavity after the developed based on the technology of the transdermal contact with less amount of saliva as compared to patch. This delivery system consists of a thin film, which dissolving tablet.[7]

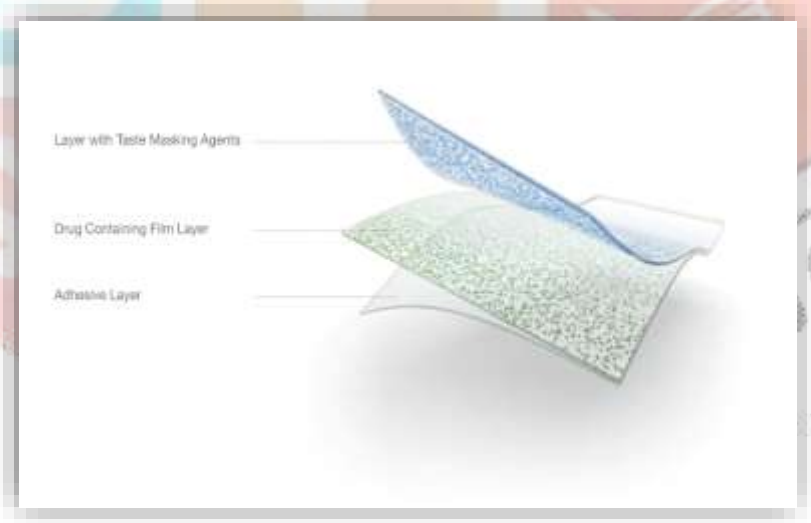

Fig.01: Oral fast dissolving films

Special features of mouth dissolving films :

1. Mouth dissolving films are thin elegant film.
2. Films are available in various sizes and shapes.
3. Film shows an excellent mucoadhesion. So, film is not detached from mouth cavity while administration.
4. It shows fast disintegration within 1 minute.
5. Drug is rapidly released from dosage form due to its fast disintegration and gives quick onset of action.[8]

Ideal characteristics of a suitable Drug candidate :

1. The drug should have pleasant taste.
2. The drug to be incorporated should have low dose upto 40 mg .
3. The drugs with smaller and moderate molecular weight are preferable .
4. The drug should have good stability and solubility in water as well as saliva .
5. It should be partially ionized at the PH of oral cavity.
6. It should have the ability to permeate oral mucosal tissue.[9]

Advantages of orally fast dissolving film:

1. No need of water for administration.
2. Convenient for pediatric, geriatric and dysphasic patients having difficulty in swallowing.
3. Rapid disintegrating and dissolution in the oral cavity due to larger surface area of films.
4. Rapid onset of action with increased bioavailability due to bypassing hepatic first pass effect.
5. Reduce dose, enhances the efficacy and safety profile of the drug with reduced side effects.
6. Flexible and portable in nature so they provide ease in handling, transportation and storage.
7. Ease of administration to mentally ill, disabled, uncooperative patients and the patients who are on reduced liquid intake plans or are nauseated.[10]

Mechanism of absorption:

Sublingual administration drug solutes are rapidly absorbed into the reticulated vein, which lies underneath the oral mucosa and transported through the facial veins, internal jugular vein, and braciocephalic vein and are then drained into the systemic circulation. Upon sublingual administration drug reaches directly in to the blood stream through the ventral surface of the tongue and floor of the mouth. The main mechanism for the absorption of the drug in to oral mucosa is via passive diffusion into the lipoidal membrane .The absorption of the drug through the sublingual route is 3 to 10 times greater than oral route and is only surpassed by hypodermic injection. [11]

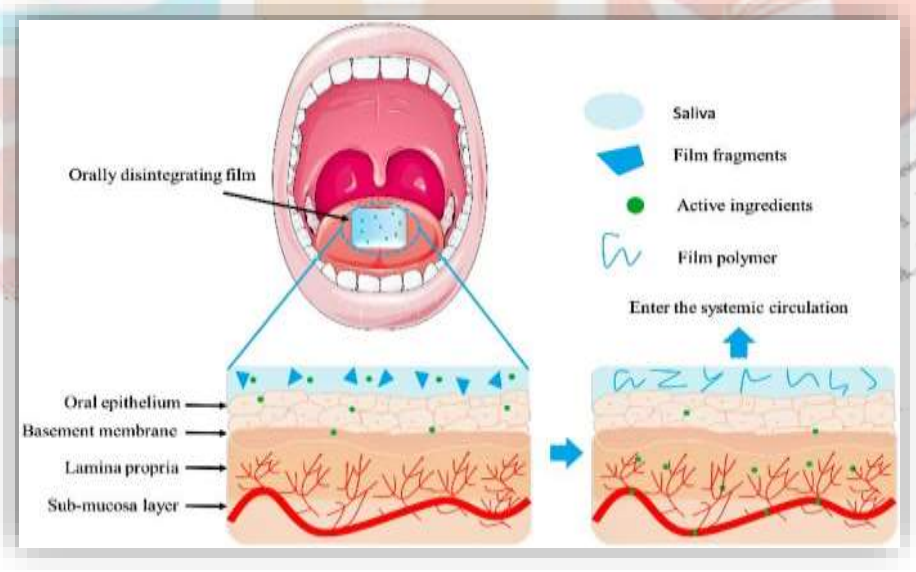

Fig.02:Mechanism of action of OFDF

MATERIALS AND METHODS

Materials:

Domperidone, Hydroxy propyl methyl cellulose, PEG4000, gellan gum , Tween 80, Methanol and water, Glycerin these were gifted by respective industries such as Morpan Pharma, and Loba Chemicals Mumbai. Sonicator used for mixing of polymers and drug.

Ingredients	F1	F2	F3	F4	F5
Domperidone	210mg	210mg	210mg	210mg	210mg
HPMC E15	500mg	750mg	1000mg	750mg	750mg
Citric acid	50mg	50mg	50mg	50mg	50mg
Tween-80	5%	5%	5%	5%	5%
Methanol	12ml	12ml	12ml	12ml	12ml
Water	10ml	10ml	10ml	10ml	10ml
PEG-400	20%	20%	20%	10%	15%

Table 1: Formulation of mouth dissolving film of Domperidone

Preparation of Domperidone FDFs using solvent casting method :
Solid dispersion of Domperidone and β-cyclodextrin (1:3) was selected and dispersed in half quantity of water and to it methanol is added
along with Tween-80 and heated at 60°C. In other half quantity of water, HPMC E15 is dissolved and PEG-400 is added. Both
the solutions are sonicated and then casted in Petri dish. It is dried in oven at 60°C for 5 hrs to obtain the film.

In vitro dissolution studies : The drug release from the prepared SD was studied using eight station dissolution rate test apparatus (Lab India, Disso 2000) employing a paddle stirrer at 75 rpm and at 37±0.5°C. Phosphate buffer of pH 6.8 (900 ml) was used as dissolution fluid. At predetermined intervals, the aliquots sample was withdrawn and replaced with fresh media. The absorbance of these solutions was measured at 284 nm using spectrophotometer. The same process was used for domperidone FDFs[12]

Evaluation of mouth dissolving films :

- **Visual Inspection :** The films were round (takes the shape of the petri dish), transparent, clear, soft, without air bubbles, uniform in thickness, colorless, thin, easily removed from the petri dish and had a good texture from all edges.[13]
- **Thickness :** The thickness of each sample was measured using calibrated ocular stage micrometer slide and microscope. Three film samples (2cm×2cm) were cut from three different locations of 63.58cm2 films and the mean thickness calculated. The film was placed in vertical position supported by two clamps below the lens.[14]
- **Weight variation test :** Weight variation was studied by individually weighing 10 randomly selected film strips and calculating the average weight by digital weighing balance.[14]
- **Surface pH of films :** The surface pH of films was determined to examine the probable side effect because of change in pH in-vivo, since an acidic or alkaline pH may irritate oral mucosa. The film to be tested was placed in a test tube and was moistened with 1 ml of distilled water and kept for 30 seconds.[15]
- **Folding endurance :**Folding endurance is determined by repeated folding of the strip at the same place until the strip breaks. The number of times the film is folded without breaking is computed as the folding endurance value.[16]
- **Disintegration time:** The assay values of all the formulations were ranging from 97.69 to 99.72 %.[17].
- **Transparency :** The transparency of the films can be determined using a simple UV spectrophotometer. The film samples are cut into rectangles and placed on the internal side of the spectrophotometer cell.[18]

RESULT:

All the films were soft, semi-transparent, and non-sticky, with smooth surfaces. Each film had a uniform weight, but varied in thickness due to different amounts of polymer, ranging from 0.14 mm to 0.36 mm. Increasing the concentration of HPMC E15 from 5% to 10% resulted in thicker strips and decreased folding endurance. The surface pH of all formulations was 6.8-7.2, preventing irritation to the oral mucosa. Prepared fast dissolving oral films formulations complied with the physical evaluation parameters like pH, Appearance, irritancy test, colour, studies were found to be acceptable which were notified in Table 2.

EVALUATION PARAMETERS	OBSERVATION
Appearance	Semi transferant
Colour	White
Odour	Odourless
PH	6.8
Irritancy	Non irritant

Table 2 : physical evaluation

TEST PARAMETERS	F1	F2	F3	F4	F5
Thickness(mm) (±0.003)	0.12	0.12	0.14	0.13	0.15
Folding Endurance	7	9	13	15	17
Tensile Strength (kg/cm2)	0.45	0.51	0.6	4.23	5.67
Disintegration time (sec)	19	23	24	53	55
Drug content(mg) (±0.005)	4.92	4.94	4.90	4.96	4.99

Table 3: Evaluation Parameters

SUMMARY AND CONCLUSION:

The main aim objective of the study was to design and evaluate fast dissolving film containing Domperidone which can be a good way to bypass the extensive hepatic first pass metabolism. The 4, 5, and 6 % w/w Pullulan films were prepared by solvent casting method. Compatibility of Domperidone with polymer was confirmed by FTIR. Three films were evaluated for weight variation and thickness showed satisfactory results. Mouth dissolving time and disintegration time of the films were increased with increase in the concentration of the polymers, as more fluid is required to wet the film in the mouth. Content uniformity study showed that the drug is uniformly distributed in the film. Present study reveals that all the three formulated films. showed satisfactory film parameters. The developed formulation disintegrates in the oral cavity within 75 seconds and improves the patient compliance particularly for those having difficulty in swallowing.

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