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Research Article

FORMULATION, OPTIMIZATION AND EVALUATION OF FAST DISSOLVING ORAL FILM OF DOMPERIDONE

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ABSTRACT

Fast dissolving dosage form (FDDF) is designed to allow administration of an oral solid dose form in the absence of water or fluid intake. Such formulation readily dissolve or disintegrate in the saliva generally within <60seconds. Fast dissolving Systems are useful for pediatric, geriatric, and bedridden patients and for patients who are suffered with Dysphasia. This fast dissolving drug delivery system (FDDS) is suited for the drugs which undergo high first pass metabolism and is used for improving bioavailability with reducing dosing frequency to mouth plasma peak levels, which in turn minimize adverse/side effects. Some drugs are absorbed well from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablet dosage form. Most fast-dissolving delivery system films must include substances to mask the taste of the active ingredient. This masked active ingredient is then swallowed by the patient's saliva along with the soluble and insoluble excipients. The sublingual and buccal delivery of a drug via oral film has the potential to improve the onset of action, lower the dosing, and enhance the efficacy and safety profile of the medicament. In this paper we have compared fast dissolving tablet and fast dissolving oral film.

Keywords: FDDF, FDDDS, Fast dissolving tablet, Bioavailability, Fast dissolving oral film

INTRODUCTION:

Despite the tremendous advancement in the drug delivery system, oral route is the most preferred route of administration and tablet and capsules are the most preferred dosage form [1-3] but now they experienced several limitations like chocking and swelling discomforts in the geriatric and paediatric patients [4-5]. Among the plethora of avenues explored oral strips gain more attention as it emerging new platform for geriatric and paediatric patients [6-8].Fast dissolving dosage forms can be disintegrated, dissolved, or suspended by saliva in the mouth. This fast dissolving tablet disintegrates instantaneously when placed on tongue and releases the drug dissolves or disperses in the saliva. Fast dissolving tablets are useful in patients, like pediatric, geriatric, bedridden, or mentally disabled, who may face difficulty in swallowing conventional tablets or capsules leading to ineffective therapy, with persistent nausea, sudden episodes of allergic attacks, or coughing for those who have an active life style. Fast dissolving tablets are also applicable when local action in the mouth is desirable such as local anesthetic for toothaches, oral ulcers, cold sores, or teething, and to those who cannot swallow intact sustained action tablets/capsules.[9]Fast dissolving drug delivery system (FDDS) was introduced in late 1970 as the alternative to conventional tablet, capsule and syrups especially for the geriatric and paediatric patients suffering from the dysphasia problem [10]. Fast dissolving tablets are the solid dosage form which disintegrates rapidly in the oral cavity without the need of water [11-12]. Some problems are associated with the OFDF like they are sometime difficult to carry, storing and handling (friability and fragility), these are prepared using the expensive lyophilisation method [13-14]. To overcome these problems oral films were developed, which are very popular now a days. The concept of oral film was come from confectionary industry [15-16]. Oral films are the recent ultrathin novel formulation of postage stamp size which contains active pharmaceutical ingredients and excipients. Domperidone is a specific blocker of dopamine receptors. It speeds gastrointestinal peristalsis, causes prolactin release, and is used as antiemetic and tool in the study of dopaminergic mechanisms. Domperidone acts as a gastrointestinal emptying (delayed) adjunct and peristaltic stimulant. The gastroprokinetic properties of Domperidone are related to its peripheral dopamine receptor blocking properties. Domperidone facilitates gastric emptying and decreases

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small bowel transit time by increasing esophageal and gastric peristalsis and by lowering esophageal sphincter pressure. Antiemetic: The antiemetic properties of Domperidone are related to its dopamine receptor blocking activity at both the chemoreceptor trigger zone and at the gastric level. It has strong affinities for the D2 and D3 dopamine receptors, which are found in the chemoreceptor trigger zone, located just outside the blood brain barrier, which - among others - regulates nausea and vomiting.

MATERIAL AND METHOD

Material

Domperidone, Sodium starch glycolate, Corn starch, Sodium CMC, Crosspovidone, Mg stereate, Mannitol, Polyvinyl alcohol, Glycerin, Electronic weighing machine, UV-VIS spectrophotometer (SHIMADZU), Friability test apparatus EF-2, Dissolution apparatus.

Formulation of Fast dissolving oral film by Solvent casting method

The oral fast dissolving film of Domperidone was prepared by solvent-casting method. Film forming polymer PVA (polyvinyl alcohol) was dissolved in 10 ml of distilled water by continuous stirring with the help of magnetic stirrer for 2 hrs in 100 ml beaker. After 2 hrs, 2 gram of glycerin and dissolved drug (Domperidone in DMSO) was incorporated into the beaker. It was further stirrer for 2 to 3 hrs. Finally the entire mixture was casted into the petri dish and allowed to dry at room temperature. The film was carefully removed from the petri dish, and cut into size of 2 cm^2.

Table no 1: List of ingredients used in the Fast dissolving oral film

Ingredients	Quantity
Domperidone	10 mg
PVA	1 – 5 % w/v
Glycerin	11 – 20 % w/v
DMSO	1 ml
Distilled water	10 ml

OPTIMIZATION OF POLYMER:

In the formulation of Fast dissolving oral film the polymer was optimized. The optimized polymer was PVA which was used as a film forming agent. The concentration of polymer was optimized from 1% - 5 % (w/v).

FORMULATION TABLE FOR FAST DISSOLVING ORAL FILM:

Table no 2: Composition of Fast Dissolving Oral Film of Domperidone:

Ingredients	N_1	N_2	N_3	N_4	N_5	N_6
Domperidone	10 mg	10 mg	10 mg	10mg	10 mg	10 mg
PVA	0.10gm	0.15gm	0.20gm	0.25gm	0.30gm	0.35gm
Glycerin	2 gm	2 gm	2 gm	2 gm	2 gm	2 gm
DMSO	1 ml	1 ml	1 ml	1 ml	1 ml	1 ml
Distilled water	10 ml	10 ml	10 ml	10 ml	10 ml	10 ml

Evaluation of fast dissolving oral film:

Visual Inspection: The fast dissolving films were inspected manually for their transparency and air bubble.

Weight variation: The four individual batches of fast dissolving film of size (2x2 cm^2) was weighted on an electronic balance and the average weight was determined.

Thickness: The thickness of film (2x2 cm^2) was measured by using a micrometer screw gauge. The thickness of each film at three different places determined [18,19,20].

Folding Endurance: The folding endurance of patches was determined byrepeatedly folding one patch at the same place till itbreak or up to 300 times without broken. Theexperiments were performed in triplicate, and averagevalues were reported [21].

Surface pH: For the determination of surface pH combined glasselectrode was used. The patches were kept in contactwith 5 ml of distilled water for 1 hr. The pH was noted by bringing the electrode near the surface offormulations and allowed it to equilibrate for 1 min.

Weight of film: The fast dissolving oral film were weighted on analytical balance (Shimadzu).

In vitro Disintegration studies: The disintegration time was performed using USP disintegration test apparatus with 6.8 phosphate buffer solution at 37 ±0.5^{0}C. Disintegration time was recorded when all the patches (2 x 2 cm$^{2)}$ of the disintegrated film (6 tablet) dissolved or passed through the screen of the basket. The time and mean value were reported

Drug content: A film of 2 x 2 cm^2 was cut and placed in a beaker containing 10 ml of 6.8 pH phosphate buffer solution. The content was stirred in magnetic stirrer to dissolve the film. The content was transferred to a volumetric flask of 10 ml. The absorbance of the solution was measured against 6.8 pH phosphate buffer as a blank solution at 287 nm [17].

In-vitro dissolution studies: The dissolution study was carried out in 100 ml of 6.8 pH phosphate buffer solution. The dissolution study was used to study the drug release from the bilayered and multilayered patches. The dissolution medium consisted of phosphate buffer pH 6.8. The drug release study was performed at 37$^{0\pm}$ 0.5°C, with a rotation speed of 50 rpm. Samples (3 ml) were withdrawn at predetermined time intervals of 2 min and replaced with fresh medium. The samples filtered through whatman filter paper and absorbance was taken at 287 nm [22].

RESULT AND DISCUSSION

PREFORMULATION STUDIES:

Drug Identification-

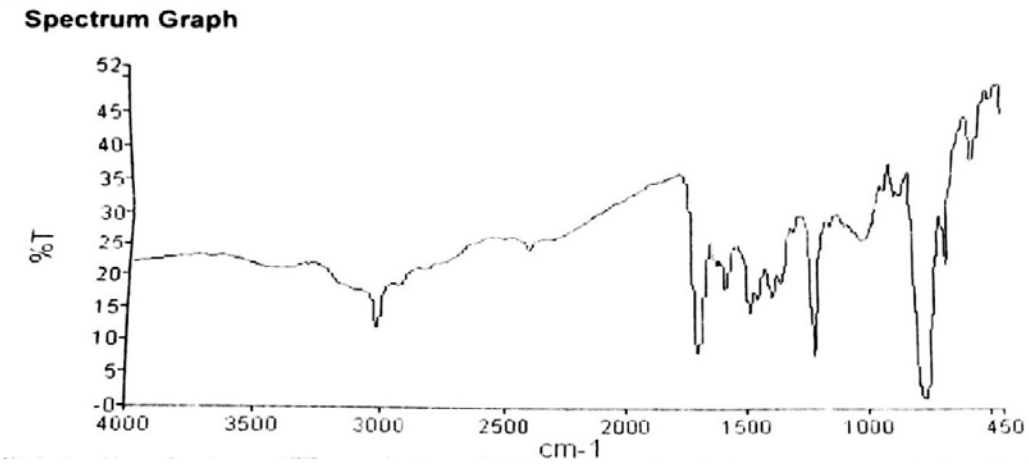

Fig no 1: FT IR spectra of Domperidone

COMPATIBILITY STUDY-

The compatibility studies were performed using IR spectrophotometer.

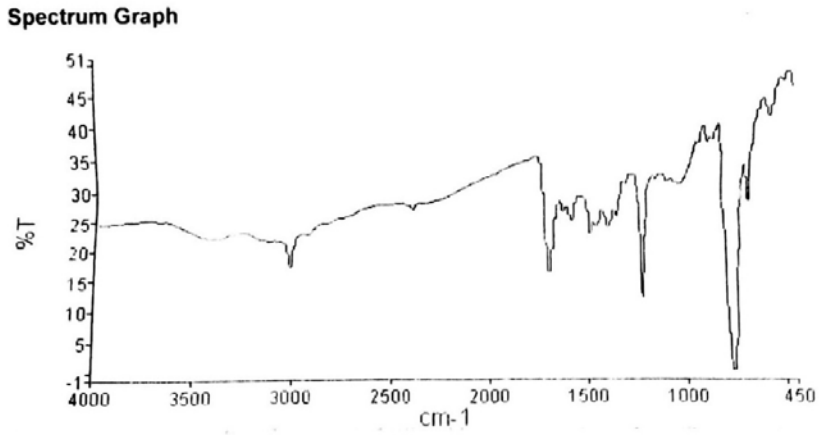

Fig no 2: FT IR spectra of Domperidone + Crosspovidone

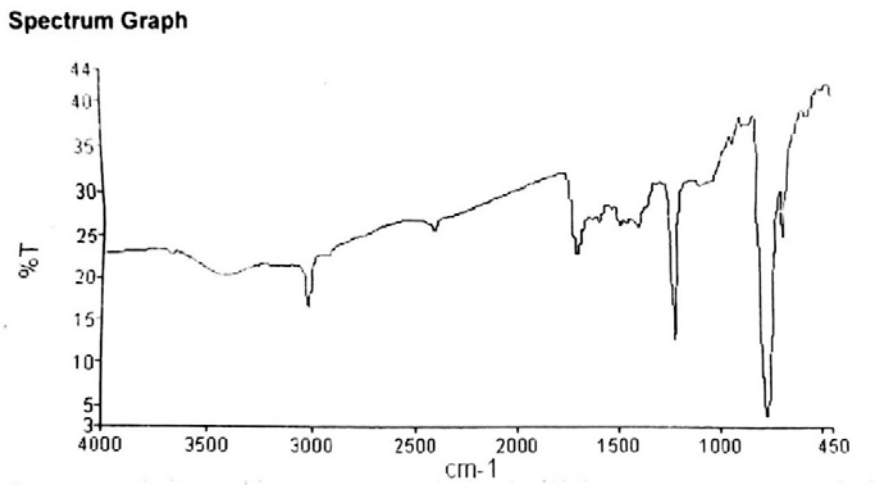

Fig no 3: FT IR spectra of Domperidone + PVA

All the significant peaks of Domperidone were present in the entire spectrum obtained between the drug and excipients. It shows that there was no significant change in integrity of the drug.

EVALUATION PARAMETERS OF FAST DISSOLVING ORAL FILM:

Visual Inspection: The visual Inspection was carried out manually which showed in Table no 3. Formulation N_3 and N_4 were transparent but formulation N_1 and N_6 were semitransparent.

Weight of film: As the weight of polymer increased, the weight of film was also increased. Weight of the film of N_2 - N_6 was found in range of 81.2 mg – 121.9 mg. Minimum weight of the film was found of the N_2 formulation which was 81.2 mg and the maximum weight of the film was 121.9 mg of N_6 formulation shown in Table no 3.

Folding endurance: The folding endurance of the film formulation by solvent casting method was found to be in range of 104 – 150. The result was shown in Table no 3.

Thickness: Thickness of the film was found in increasing order. As polymer concentration increased the thickness of the film also increased as shown in Table no 3. Film thickness of formulation N_2 – N_6 was found to be in range of 136 - 189µm.

Disintegration time: Disintegration time was found in range of 26 second to 35 seconds shown in Table no 3. Disintegration time for formulation N_4 was found 26 seconds as fastest and for N_6 was 35 seconds as slowest.

Surface pH: The pH of the film was found in the range of 6.0– 7.6 for all formulation. The result was showed in Table no 3.

Drug content: The percentage of drug content was found to be in range of 89.7 – 98.6 of Domperidone, which was within acceptable limits. Table no 3 showed the results of drug content in each batch.

Dissolution studies: The dissolution studies of the formulation batches from N_2 – N_6 were carried out to know the in-vitro drug release. The drug release at different time intervals was determined and calculated to know the release at variable concentration of polymer used. The results were converted in form of % drug release. For formulation N_4 the dissolution time was 10 min in which 98.7% drug was release.

Table no 3: Evaluation tests for Fast dissolving film

Batch	Visual appearance	Thickness of film (µm)	Disintegration Time (sec)	Folding endurane	Weight of Film (mg)	pH	Drug Content(%)
N_2	Semi Transparent	136	28	104	81.2	7.3	89.7
N_3	Transparent	154	31	127	95.6	6.4	95.2
N_4	Transparent	173	26	148	105.8	6.2	98.6
N_6	Semi Transparent	189	35	150	121.9	7.6	97.3

Dissolution profile;

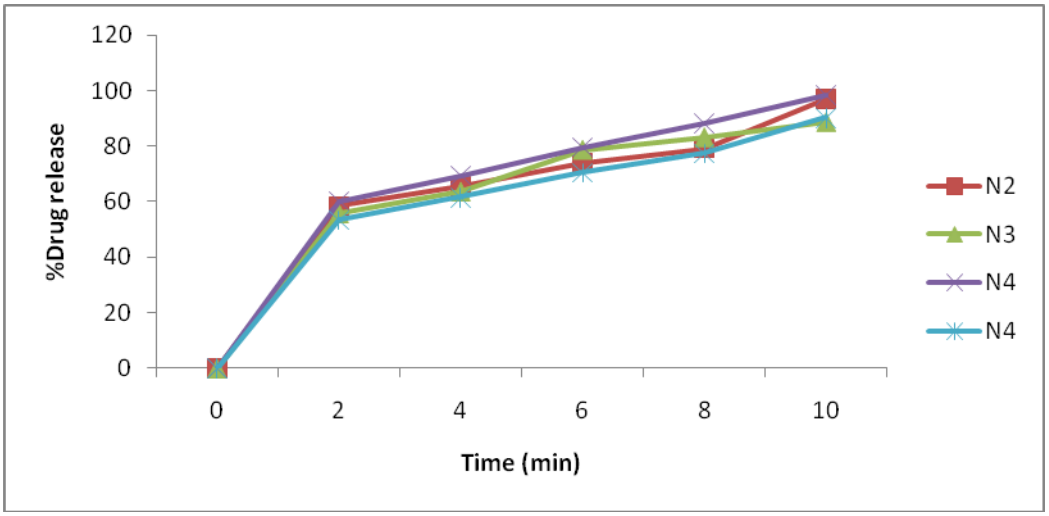

Fig no 4: Comparative percentage Drug release vs. Time for all batches of Fast dissolving film

The comparative percentage Drug release was shown in Fig no 4. Among all the batches, N_4 batch achieved maximum percentage drug release at the end of 10 minutes. Therefore formulation N_4 was the best formulation for Fast dissolving oral film of Domperidone. The drug release for the batch N_4 (MDF) was 98.7 % at the end of 10 minutes. Hence Fast dissolving film is producing rapid action and provide fast relief in case of nausea and vomiting.

DISCUSSION:

The Fast dissolving oral film of Domperidone was prepared by Solvent casting method. Formulation of film was carried out using film forming polymer (PVA), plasticizer, DMSO and distilled water. The optimization of concentration of polymer was performed for least disintegration time and good drug release as well. Taste and odour was acceptable for both types of patient like geriatric and pediatric. The obtained calibration curve was straight line. The curve was obtained in 0.1N HCl at the maximum wavelength of 287 nm. The slope, intercept and regression coefficient were obtained from the graph. The calculation of in-vitro drug release study was based on the calibration curve.Compatibility studies of Domperidone with different excipients and polymer were carried out prior to the preparation. All the significant peaks of Domperidone were present in the entire spectrum obtained between the drug and excipients. It shows that there was no significant change in integrity of the drug.

CONCLUSION:

The aim of this study was to prepare and Evaluate the Fast dissolving film of Domperidone drug as an anti-emetic drug. Solvent casting method was used for the formulation of Fast dissolving oral film of Domperidone. Fast dissolving oral films are beneficial for geriatric and pediatric patients. For the Fast dissolving oral film formulation N_4 is the best formulation among all formulation. The disintegration time and in-vitro drug release is good. About 98.7% drug was released within 10 minutes by Solvent casting method. The percent drug release of Fast dissolving film (N_4) was 98.7 % at the end of 10 minutes and the disintegration time was 28 seconds. Therefore on the basis of percentage drug release and disintegration times the Fast dissolving film of Domperidone was produce rapid action and provide relief in case of nausea and vomiting.

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