Design and In-vitro Characterization of Domperidone Oral Thin Films

Dasari Deepthi*[1], Angilicam Avinash[2], Dr. M. Krishnaveni[2]
[1]*M. Pharmacy 2nd Year, Narayana Pharmacy College, Nellore, Andhra Pradesh, India-524003*
[2]*Department of Pharmaceutics, Narayana Pharmacy College, Nellore, Andhra Pradesh, India-524003*

Abstract- Domperidone is a medication used as an antiemetic, gastric prokinetic agent, and galactagogue. It may be taken by mouth, and is available as a tablet, orally disintegrating tablets, suspension, and suppositories. The drug is used to relieve nausea and vomiting; to increase the transit of food through the stomach (by increasing gastrointestinal peristalsis); and to promote lactation (breast milk production) by release of prolactin. In present study oral thin films of Domperidone were developed to have a faster on set of action. The oral thin films were developed by using polymers sodium alginate, xanthan gum and PVP K30. Oral thin films were prepared by employing solvent casting method. Propylene glycol was selected as permeation enhancer and plasticizer. Drug excipient compatibility studies were carried out by using FTIR, and it was observed that there were no interactions. Formulations were prepared with the varying concentrations polymers ranging from F1-F6, and all the formulations were evaluated for various physical parameters Physical appearance, Weight variation, Thickness, Folding endurance, Tensile strength, Drug content, Moisture uptake, Moisture content and all the results were found to be were found to be within the pharmacopeial limits, in-vitro drug release studies by using dialysis membrane. Among all the 6 formulations F5 formulation which contain PVP K30 50 mg and shown 98.06% cumulative drug release within 30 min. And compared to sodium alginate, xanthan gum and PVP K30, sodium alginate showed better drug release profile.

Key words: Domperidone, sodium alginate, xanthan gum and PVP K30.

INTRODUCTION

Recent developments in the technology have presented viable dosage alternatives from oral route for pediatrics, geriatric, bedridden, nauseous or noncompliant patients. Buccal drug delivery has lately become an important route of drug administration. Various bioadhesive mucosal dosage forms have been developed, which includes adhesive tablets, gels, ointments, patches and more recently the use of polymeric films for buccal delivery, also known as mouth dissolving films. Mouth dissolving films, a new drug delivery system for the oral delivery of the drugs, was developed based on the technology of the transdermal patch. [1] The delivery system consists of a very thin oral strip, which 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. It then rapidly disintegrates and dissolves to release the medication for oromucosal absorption or with formula modifications, will maintain the quick-dissolving aspects allow for gastrointestinal absorption to be achieved when swallowed. In contrast to other existing, rapid dissolving dosage forms, which consist of liophylisates, the rapid films can be produced with a manufacturing process that is competitive with the manufacturing costs of conventional tablets. [2]

Domperidone is a dopamine antagonist it acts as a gastrointestinal emptying (delayed) adjunct and peristaltic stimulant. The gastroprokinetic properties of domperidone are connected to its peripheral dopamine receptor blocking properties. Domperidone enables gastric emptying and decreases small bowel transfer time by increasing oesophageal and gastric peristalsis and by lowering oesophageal sphincter pressure. 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. Buccal delivery of domperidone might be used as an alternative route to overcome the

disadvantages of its oral administration. Therefore objective of present work was to design and evaluate oral thin films of domperidone by solvent casting method to improve its solubility and make it suitable for the treatment of nauseous and vomiting patients. [3]

MATERIALS AND METHODS

Materials

Domperidone (NATCO LABS), PVP K30, Propylene Glycol, Aspartame (Merck Specialties Pvt. Ltd, Mumbai), Sodium alginate, Xanthan gum, Citric Acid (SD fine chemicals, Mumbai).

Formulation of Domperidone Oral thin films:

Oral thin films were prepared by solvent casting method. Sodium alginate xanthan gum and PVPK 90 were weighed in required ratios and they were then dissolved in water (Cold water) as solvent. Domperidone (100mg), Propylene glycol was added to the above dispersion under continuous stirring. The uniform dispersion was poured in the petri plate. The rate of evaporation of solvent was controlled by inverting cut funnel over the thin films. After 24h, the dried thin film were taken out and stored in desiccator. [4]

Table 1: Formulations of Domperidone oral thin film

S.No	Ingredients	F1	F2	F3	F4	F5	F6
1	Domperidone (mg)	100	100	100	100	100	100
2	Sodium alginate (mg)	50	100	---	---	---	---
3	Xanthan gum (mg)	---	---	50	100	---	---
4	PVP K30 (mg)	---	---	---	---	50	100
4	Propylene glycol(ml)	0.3	0.3	0.3	0.3	0.3	0.3
5	Citric Acid (mg)	0.1	0.1	0.1	0.1	0.1	0.1
6	Aspartame (mg)	0.1	0.1	0.1	0.1	0.1	0.1
6	Water(ml)	30	30	30	30	30	30

Evaluation of oral thin film

Organoleptic evaluation:

For evaluation of psychophysical evaluation of the product, special controlled human taste panels are used. In-vitro methods of utilizing taste sensors, specially designed apparatus and drug release by modified pharmacopoeial methods are being used for this purpose. These in-vitro taste assessment apparatus and methodologies are well suited for high-throughput taste screening of oral pharmaceutical formulations. [5]

Thickness measurement:

Thickness of the film is measured using a dial gauge tester. Thickness at different points is measured from which the average thickness of the fast dissolving oral films was determined. [6]

Disintegration time:

It is the time at which the film begins to break down when brought into contact with water. It can be determined by keeping a film of desired size in a Petri dish containing water and noting the time it takes to break down.

Measurement of folding endurance:

In order to carry out the endurance study, the strip of film is repeatedly folded at the same place until it breaks. The number of times the film is folded at the same place prior to breaking gives the folding endurance. [7]

pH

pH measurement is carried out by keeping the film in contact with distilled water, and after 1 hour, the pH of the solution or dispersion is measured.

Content uniformity

The drug content was performed to ensure the drug loading onto each film. This test was performed by dissolving a 6 cm26.8 phosphate buffer with stirring. The resultant solution was filtered using a whatman filter paper, and the filtrate was diluted to 100 ml with the same buffer in a volumetric flask. Then 1 ml of the filtrate was further diluted to 10ml with buffer. This solution was analyzed using a spectrophotometer at 261 nm. The content uniformity test was used to ensure that every film contains the intended amount of drug substance with little variation among films area of film in 50 ml of a film. Three pieces, each 6

cm2cm), were cut from the whole patch, and assayed for drug content. Same procedure was repeated for all the six batches. [8]

In vitro dissolution study

The in vitro drug release study of film was carried out using a USP 23 type 2 rotating paddle dissolution test apparatus. 250ml of phosphate buffer (pH 6.8) was used, and maintained at 37±5°C while the basket was set at 50 rpm. A film sample of 4 $cm^2$was fixed onto the specially designed SS disk with the help of cyanoacrylate adhesive. The disk was put at the bottom of the dissolution vessel so that the patch remained on the upper side of the disk. Five milliliters of samples were taken at a interval of 60 sec., and the same amount was replaced with fresh buffer. The withdrawn samples were filtered through whatman filter paper and then 1ml of the filtered sample was further diluted to 10ml of the same medium and analyzed using a spectrophotometer at a wavelength of 261 nm. The cumulative percentage release for different formulations was calculated. The relationship between time and percentage release were plotted. The results of in- vitro dissolution studies of all formulations [9].

Moisture uptake:

The test is done by keeping previously weighed films in desiccators at a particular temperature and relative humidity. After three days, the film is taken out and reweighed to determine the percentage of moisture uptake. Percentage of moisture uptake can be calculated as follows.

$$\text{Percentage of moisture uptake} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

Moisture content:

Previously weighed films are stored in a desiccator for 24 hours. The final weight is noted when there is no further change in the weight of individual film. Percentage of moisture content can be calculated as follows,

$$\text{Percentage of moisture content} = \frac{\text{Initial weight} - \text{Finalweight}}{\text{Initial weight}} \times 100$$

Tensile strength:

Tensile strength is the maximum stress applied to a point at which the strip specimen breaks. Tensile strength of the film is determined by using a tensile testing machine like the Instron or Monsanto tester. [10]

Swelling Property:

Film swelling studies are conducted using a simulated saliva solution. Each film sample is weighed and placed in a pre weighed stainless steel wire mesh. The mesh containing film sample is submerged into a 15 ml medium in a plastic container. An increase in the weight of the film was determined at preset time intervals until a constant weight was observed.

Degree of swelling property is calculated by following formula,

$$\text{Swelling Index (SI)} = (Wt - Wo) / Wo.$$

Where, Wt is the weight of the film at time "t" and Wo= weight of the film at t = 0.

Drug excipients interaction studies:

IR spectral analysis was carried out using FT-IR by the KBr disc method. The sample and KBr were triturated and compressed to get the discs. The samples of pure drug, dummy formulation and optimized formulation were analyzed between wave numbers 4000.0 and 400.0 cm^{-1}. [11]

RESULTS & DISCUSSION

It was found that the estimation of Domperidone by UV spectrophotometric method at λ_{max} 261 nm in 6.8 pH saline phosphate buffer and had good reproducibility and this method was used in the study. The correlation coefficient for the standard curve was found to be closer to 1, at the concentration range, 1-6 µg/ml.

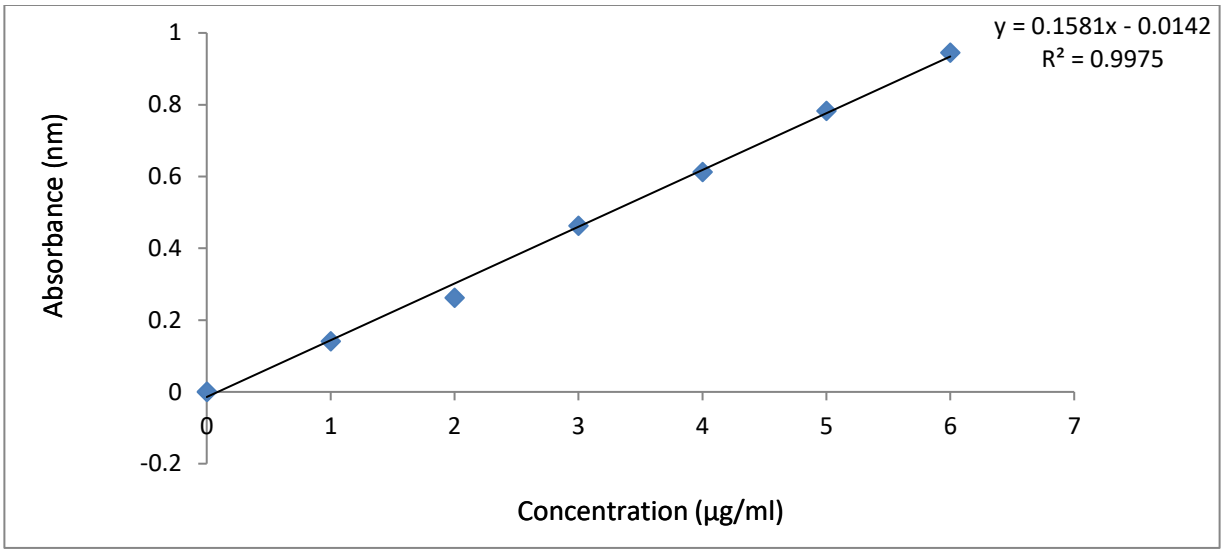

Fig 1: Standard graph of Domperidone in pH 6.8 Phosphate buffer

Evaluation of Domperidone oral thin films:

Physical appearance: All the Oral thin films were visually inspected for colour, clarity, flexibility.

Flatness: All the Oral thin films were found to be flat without any foam.

Table 2: Evaluation of Oral thin films by physical methods

Formulation code	Thickness (mm)	Folding endurance	Drug content (%)	Moisture uptake (%)	Moisture content (%)	Weight variation
F1	0.3581	242	97.21	4.16	4.13	181.26
F2	0.3556	239	98.23	3.98	4.06	231.18
F3	0.3582	231	98.19	4.12	3.98	180.34
F4	0.3576	241	97.15	4.09	4.11	2321.92
F5	0.3569	243	97.36	3.96	3.97	179.13
F6	0.3577	242	98.27	4.05	4.15	231.15

The prepared Domperidone Oral thin films were evaluated by physical methods such as Physical appearance, Weight variation, Thickness, Folding endurance, Drug content, Moisture uptake and Moisture content and all the results were found to be within the pharmacopeial limits.

Tensile strength (F5):

The optimised film (F5) was dried at 60^0C for 24 hrs. Then they were placed in an isometric transducer and the force required for their rapture was measured by an oscillograph. The tensile strength of the oral film was found to be 1.42 gm/cm^2.

Table 3: Disintegration time and pH

Formulation code	Disintegration Time (Sec)	pH
F1	48	6.9
F2	52	6.9
F3	51	7.0
F4	52	7.1
F5	49	7.1
F6	50	6.9

The surface pH of domperidone mouth dissolving films was determined in order to investigate the possibility of any side effects in vivo. As an acidic or alkaline pH may cause irritation to the oral mucosa, it was determined to keep the surface pH as close to neutral as possible. A combined pH electrode was used for this purpose. Domperidone mouth dissolving films showed surfaces pH ranging from 6.9 to 7.0, hence the films will not cause any irritation to oral mucosa. The disintegration time of the mouth dissolving films was done by Petri dish method and was found to be in the range of 48-52 seconds.

In vitro dissolution study

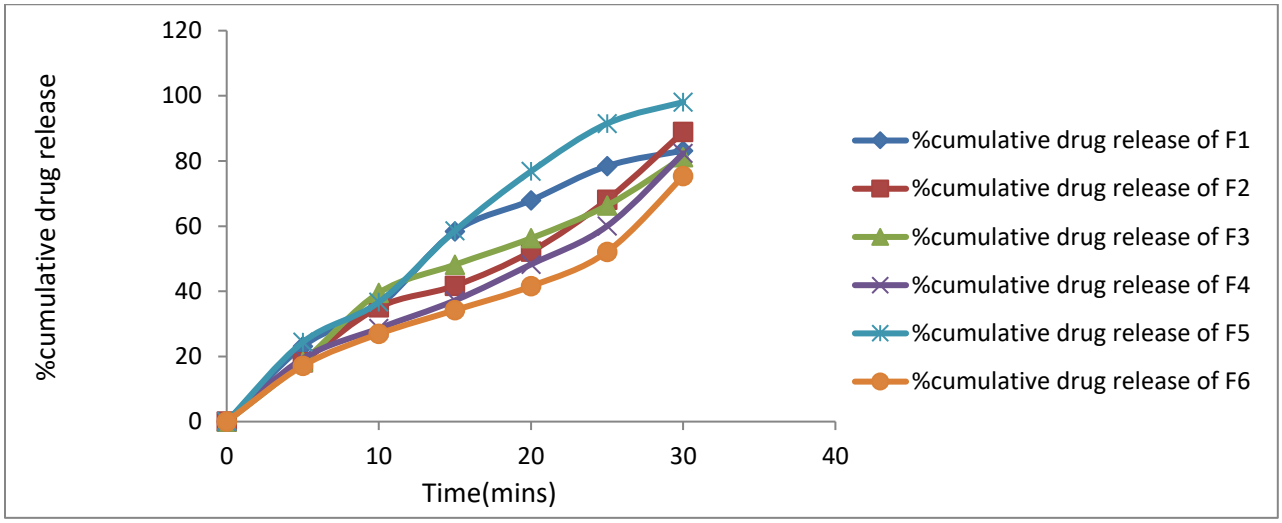

Fig 2: Dissolution graph of all formulations (F1-F6)

The prepared Domperidone oral thin films were evaluated for *In-vitro* drug release studies, Among all the 6 formulations F5 formulation which contain PVPK30 had shown 98.06% cumulative drug release with in 30 min.

Fourier transform infrared spectroscopy studies

The FTIR spectrum of the pure drug domperidone and excipients showed the characteristic absorption bands in the IR region. It is observed from the IR spectra of pure drug domperidone and optimized formulation values of significant peaks in the respective compounds have resolved in their respective expected regions, indicating that all the above compounds used are in pure state. Hence it is evident that there is no interaction of the drug with excipients. The results are shown in fig. 3 and 4.

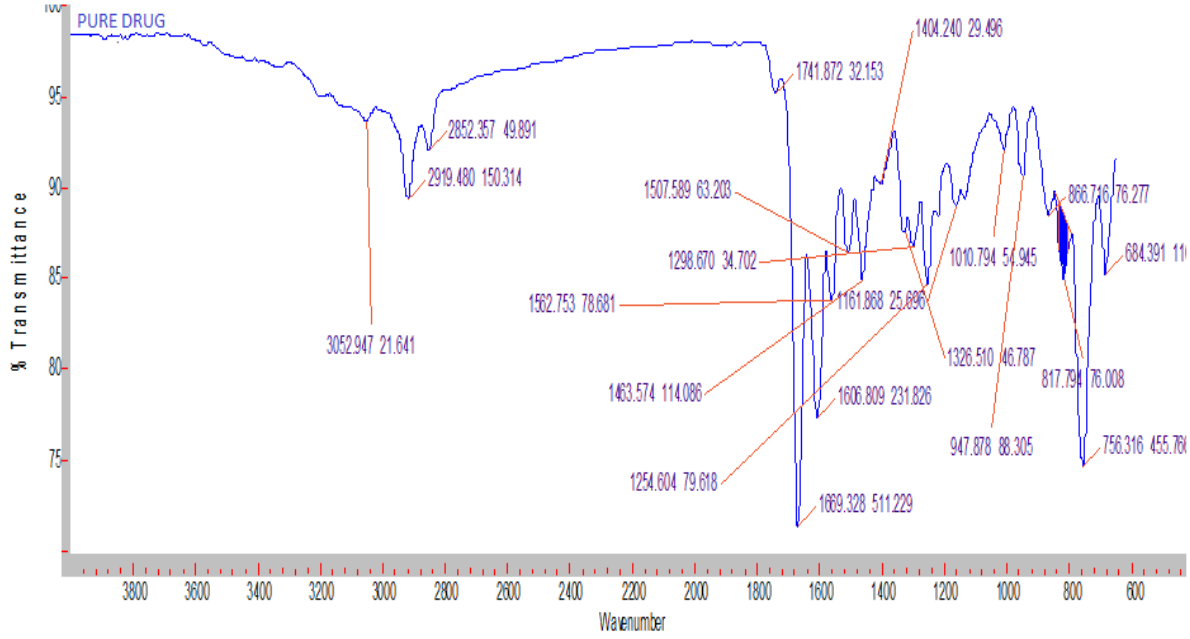

Fig 3: FTIR spectrum of pure drug

Fig 4: FTIR spectrum of optimized formulation

CONCLUSION

In present study oral thin films of Domperidone were developed to have a faster on set of action. The oral thin films were developed by using polymers sodium alginate, xanthan gum and PVP K30. Oral thin films were prepared by employing solvent casting method. Propylene glycol was selected as permeation enhancer and plasticizer. Drug excipient compatibility studies were carried out by using FTIR, and it was observed that there were no interactions. Formulations were prepared with the varying concentrations polymers ranging from F1-F6, and all the formulations were evaluated for various physical parameters like physical appearance, weight variation, Thickness, Folding endurance, Tensile strength, Drug content, Moisture uptake, Moisture content and all the results were found to be were found to be within the pharmacopeial limits, in-vitro drug release studies by using dialysis membrane. Among all the 6 formulations F3 formulation which contain PVP K30 50mg and shown 98.06% cumulative drug release within 30 min. And compared to sodium alginate, xanthan gum and PVP K30, sodium alginate showed better drug release profile.

ACKNOWLEDGEMENT

I am thankful to the Principal, Dr. K. Harinadha Baba, Narayana Pharmacy College, for providing facility to carry out the research work.

REFERENCE

[1] PagillaPragathi, Vishnu P, KondeAbbulu. Formulation and evaluation of lovastatin oral disintegration thin films. GSC Biological and Pharmaceutical Sciences, 2018; 03(02): 35–42.

[2] Muhammad Irfan, Sumeira Rabel, Quratulain Bukhtar, Muhammad Imran Qadir, Farhat Jabeen, Ahmed Khan. Orally disintegrating films: A modern expansion in drug delivery system. Saudi Pharmaceutical Journal, 2016; 24: 537–546.

[3] Julie Mariam Joshua, R Hari, Fithal K Jyothish, Saritha A Surendran. Fast Dissolving Oral Thin Films: An Effective Dosage Form for Quick Releases. Int. J. Pharm. Sci. Rev. Res., 2016; 38(1): 282-289

[4] Dipal Patel, Mihir Patel, Pratik Upadhyay, Nihar Shah, Shreeraj Shah. A Review on Mouth Dissolving Film, JPSBR, 2015; 5(3): 266-273.

[5] Mundhe Bhagyashri, Kadam Vaishali, Jadhav Suryakant, Md. Zamiruddin, Bharkad Vishvanath. A Short Review on Fast Dissolving Oral Film. World Journal of Pharmacy and Pharmaceutical Sciences, 2014; 3(3): 2-14.

[6] Jaysukh J Hirani, Dhaval A Rathod, Kantilal R Vadalia. Orally Disintegrating Tablets: A Review. Tropical Journal of Pharmaceutical Research, 2009; 8 (2): 161-172.

[7] Priya Vijaysingh Bais, Dr. Kanchan P. Upadhye and Gouri Dixit. Formulation and Evaluation of Fast Dissolving Oral Melt-In-Mouth of Lorazepam for Sublingual Use. World Journal of Pharmacy and Pharmaceutical Sciences, 2016; 5 (3):25-35.

[8] AnjumPathan, Mahesh Kumar Gupta, Neetesh Kumar Jain, Ankita Dubey, Ankit Agrawal. Formulation and Evaluation of Fast Dissolving Oral Film of Promethazine Hydrochloride Using Different Surfactants. JIPBS, 2016; 3(1): 74-84.

[9] Rahul A Jain And Atish S Mundada. Formulation, Development and Optimization of Fast Dissolving Oral Film Of Montelukast Sodium . Int J Drug Dev& Res, 2015, 7:4-12.

[10] A. Deepthi, B. Venkateswara Reddy and K. Navaneetha. Formulation and Evaluation of Fast Dissolving Oral Films of Zolmitriptan. AJADD [2014; 2(2):153-163.

[11] Pardeep Kumar Jangra, RajniBala, N.S. Gill. Development and Characterization of Fast Dissolving Oral Films of Thiocolchicoside. International Journal Of Recent Advances In Pharmaceutical Research, 2014; 4(4): 51-64.