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DESIGN AND EVALUATION OF MOUTH DISSOLVING FILM OF DOMPERIDONE USING SYNTHETIC AND NATURAL POLYMERS.

V.Kamalakkannan[1], B.Sangameswaran[2], V.Subramanian[3], A. Syed Irfan[4], V.Tamilarasan[5]

V. Kamalakkannan[1] Professor, Department of Pharmaceutics, SSM College of Pharmacy, Bhavani (Tk), Erode (DT), TamilNadu.

B.Sangameswaran[2] Principal & Director, SSM College of Pharmacy, Bhavani (Tk), Erode (DT), Tamilnadu.

V.Subramanian[3] , A. Syed Irfan[4] , V.Tamilarasan[5], Final year B.Pharm Students, SSM College of Pharmacy, Bhavani (Tk), Erode Dist, TamilNadu.

ABSTRACT

The present work aimed at preparing mouth dissolving film of Domperidone with the purpose of developing a dosage form for a very quick onset of action, which is very convenient for administration, without the problem of swallowing and using water. Mouth dissolving film of Domperidone were prepared using synthetic and natural polymers via PVA and sodium alginate as film forming agents and PEG-400 as plasticizer by solvent casting method. The major advantage of the preparation technique includes fewer operation units, better content uniformity The Mouth dissolving film formed was additionally found to be disintegrated within 1 min. The ratio of components in the Aqueous phase affected the thickness, drug content, tensile strength, percentage elongation, folding endurance, and release profile of Mouth dissolving film and the best results were obtained at DN2 formulation. Dissolution of prepared mouth dissolving film of Domperidone was performed using singhla apparatus in pH 6.8 phosphate buffer medium at 50 rpm with temperature being maintained at 37±0.5°C. The film prepared were evaluated for various parameters like thickness, weight variation, drug content uniformity, surface pH, folding endurance, disintegration time and in vitro drug release and were showed satisfactory results.

Keywords: Mouth dissolving film, Domperidone, Poly vinyl alcohol, Sodium alginate, PEG-400.

INTRODUCTION

Among all the routes that have been investigated for the systemic delivery of pharmaceuticals via diverse pharmaceutical products of varied dose forms, oral drug delivery has been recognised for a decade as the most frequently used route administration. The oral route may have gained popularity due in part to its simplicity of administration as well as the conventional wisdom that the medicine is well absorbed when administered orally[1], just like the meals that are consumed on a regular basis. For paediatric, geriatric, bedridden, queasy, or noncompliant patients, recent technological advances have made it possible to administer medications in ways that are equally effective as the oral route.

Recent years have seen a rise in the importance of buccal medication delivery. The use of polymeric films for buccal distribution, also known as mouth dissolving films, and other bio adhesive mucosal dosage forms, such as sticky tablets, gels, ointments, patches, and more recently, mouth dissolving films, have also been created[2]. When a dosage form is placed on the tongue or in the oral cavity, it quickly hydrates, adheres, and dissolves to release the medicine. This type of dosage form is referred to as a film or strip. They are also referred to as fast-melting, quick-dissolving, mouth-dissolving, and fast-dispersing films. It makes it possible for the medicine to be injected intra-gastrically or administered sublingually, both of which hasten the onset of the drug's actions. [3]

Materials and Methods:

Domperidone (drug) gift sample from Apex formulations, Chennai, PVA, Sodium alginate (film former) and PEG-400 (plasticizer) gift samples from Best Care Formulations, Pondicherry, Sucrose (Sweetener) Nice Chemicals, Mumbai, Sodium Starch Glycolate (Super Disintegrant) from Nice Chemicals, Mumbai, Menthol (flavour), Ethanol from Nice Chemicals, Mumbai, Distilled Water from Scientific suppliers, Salem.

Methods:

PREFORMULATION STUDY

Organoleptic properties [4]

The received sample of Domperidone was examined for its appearance, colour and odour.

UV Spectroscopy study: [5]

Domperidone was produced as a stock solution in phosphate buffer at pH 6.8, and its absorption maxima (λ max) were determined by measuring the UV spectrum of a 10 µg/ml solution.

Calibration curve of Domperidone

With 10 ml of water, 10 mg of drug that had been precisely measured was dissolved. Domperidone solution of 20 g/ml was created from the principal stock solution using phosphate buffer solution. The range of this solution's scan was 200–400 nm.

FT-IR Spectroscopy study [6]

Using potassium bromide powder, FTIR spectra of pure Domperidone and physical mixtures of drug-polymer, drug-excipients were produced. The apparatus was operated in dry air purge, and the scan was taken across an area of 4000-400cm^{-1} at a scanning speed of 2mm/sec with a resolution of 4 cm^{-1}. The scan was assessed for the existence of the main drug peaks, for drug peak shifting and disappearance, and for the formation of additional peaks brought on by interactions with solid dispersion agents.

PREPARATION OF DOMPERIDONE MOUTH DISSOLVING FILMS: [7]

The water soluble polymers are first dissolved in water at 1,000 rpm in the solvent casting procedure. The remaining excipients flavourings, sweeteners, etc. are all dissolved separately. The resulting solutions are then fully combined while being stirred at 1,000 rpm. The API that has been dissolved in a suitable solvent is added to the resulting solution. A vacuum is used to extract the trapped air. The finished mixture is cast into a film, allowed to dry, and then it is cut into the required number of pieces. The table 1 lists the formulation codes.

Table No 1: Composition of fast dissolving films of Domperidone using Natural and Synthetic Polymer (DS1-DS3 & DNI-DN3)

S. No	Ingredients	Formulation code					
		DS1	DS2	DS3	DN1	DN2	DN3
1	Domperidone (mg)	10	10	10	10	10	10
2	PVA(gm)	0.2	0.25	0.30	-	-	-
3	Sodium Alginate(gm)	-	-	-	0.75	1.0	1.25
4	PEG-400(ml)	2	2	2	2	2	2
5	Sodium starch Glycolate(mg)	10	10	10	10	10	10
6	Sucrose(mg)	20	20	20	20	20	20
7	Menthol(mg)	5	5	5	5	5	5
8	Ethanol(ml)	2	2	2	2	2	2
9	Distilled water(ml)	10	10	10	10	10	10

EVALUATIONS

Weight variation: [8]

Oral films were weighed on an analytical scale, and the average weight of each film was calculated. Films should have a weight that is essentially consistent. Making ensuring a film has the right number of excipients and API is helpful.

Thickness of films: [9]

The Thickness of the film was measured using a micrometre screw gauge at five distinct locations, and an average of three readings was derived. The precision of the dosage in the film is closely connected to the uniformity of film thickness, hence this is crucial to establish.

Folding endurance: [10]

Repeated folding of the strip at the same location until the strip breaks was used to measure folding endurance. The folding endurance value is calculated as the number of times the film could be folded without breaking.

Drug content uniformity: [11]

Any standard assay technique specified for the specific API in any of the standard pharmacopoeia can be used to ascertain this. By measuring the API content in each individual strip, content consistency is assessed. 85-115% is the maximum content uniformity.

Surface pH: [12]

pH evaluation: As an acidic or alkaline pH may irritate the oral mucosa, the surface pH of the Domperidone MDFs was measured to evaluate any potential adverse effects brought on by a change in pH in vivo. The pH metre was used to determine the surface pH. According to Table No. 8, the pH of compounded MDFs' surfaces was determined to be between 6.1 to 7.5, which means they were in the neutral pH range and wouldn't irritate the mouth when used. The test film was put in a Petri dish, wet with 0.5 ml of distilled water, and allowed to stand for 30 seconds. After putting the electrode of the pH metre into touch with the formulation's surface and giving it a minute to equilibrate, the pH was recorded. For each formulation, an average of three determinations were made.

In Vitro Disintegration Test: [13]

When an oral film comes in touch with saliva or water, it begins to disintegrate at that point. The time of disintegration should be in the range of 5 to 30 seconds for a fast-dissolving film. Disintegration time was investigated using a USP (United States Pharmacopoeia) disintegration device. Another approach involved dipping the film in 25 ml of water in a beaker to visually assess the disintegration time. The beaker was gently shaken to determine when the film began to crack or degrade.

In Vitro Dissolution Study: [14]

Franz diffusion cells with a dialysis membrane were used for in vitro drug release research. Both a donor compartment and a receptor compartment are present. As a diffusion medium, 900 ml of phosphate buffer 6.8 pH solution were placed within the receptor compartment. The produced film was placed in the receptor compartment while the temperature was maintained at 37±0.5°C and the medium was constantly agitated at 50 rpm using magnetic beads. At regular intervals, a 1ml sample of receptor fluid was taken out and replaced with the same volume of 1ml phosphate buffer solution. Using a SHIMANDZU spectrophotometer, the material was spectrophotometrically examined at 284 nm. The total allowable drug intake was computed and shown against time.

RESULT AND DISCUSSION

MORPHOLOGICAL PROPERTIES

Properties such as homogeneity, colour, transparency and surface of the oral films were evaluated by visually inspection

Table No: 2 Surface Properties of Domperidone

S. No	Formulationcode	Surface
1	DS1	Smooth, Transparent
2	DS2	Smooth, Transparent
3	DS3	Air bubble
4	DN1	Smooth, Transparent
5	DN2	Smooth, Transparent
6	DN3	Smooth, Transparent

Table presents the calibration curve of Domperidone in pH 6.8 phosphate buffer. The drug amount was analyzed by using UV method.

Table No: 3 Standard calibration curve of Domperidone in pH 6.8 phosphatebuffer

S.No	Concentration (µg/ml)	Absorbance(nm)
1	0	0.00
2	2	0.088
3	4	0.133
4	6	0.210
5	8	0.351
6	10	0.432
7	12	0.604

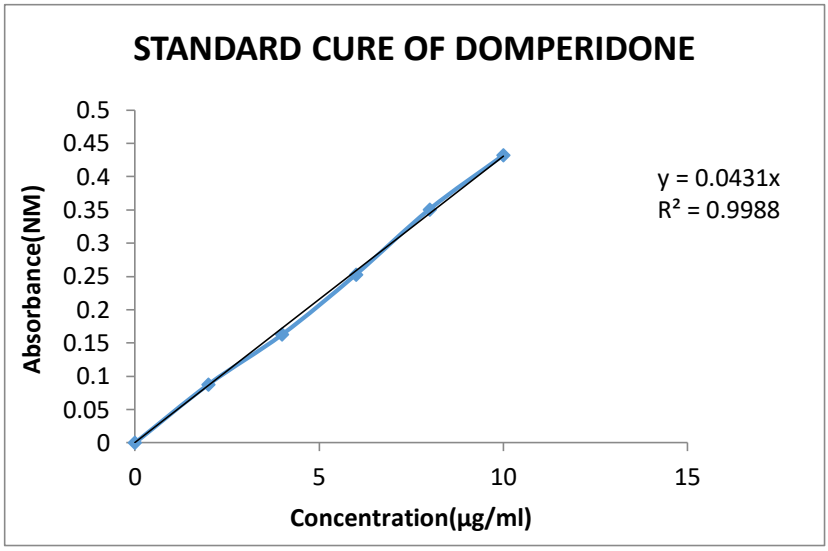

Fig 1: Standard curve of Domperidone

Drug –Polymer compatibility studies by FTIR:

The FTIR spectra of Domperidone, and the combination of drug and polymers were shows no significant interaction between drug and polymer. The FTIR spectra's of Domperidone and mixture of drug along with polymers are shown in figure 2 &3..

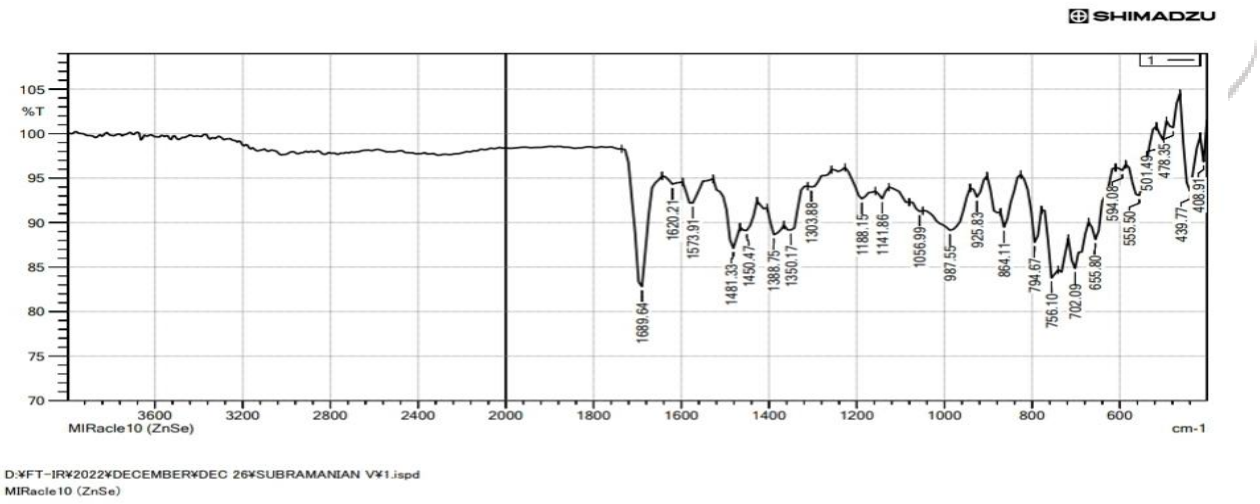

Fig 2: FTIR Spectra of Domperidone

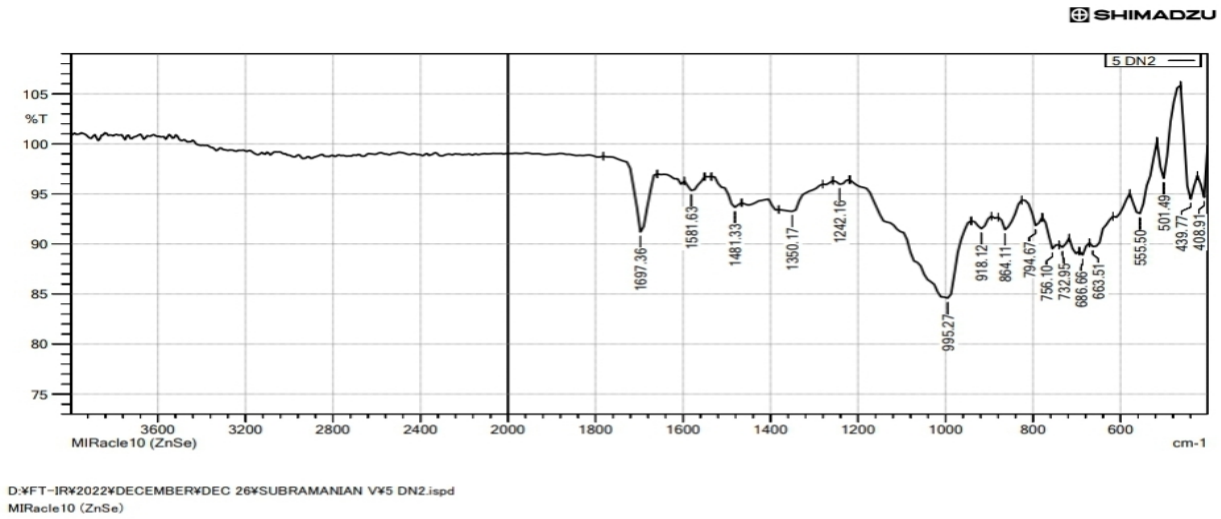

Fig 3: FTIR Spectra of DN2

Fig 4: Formulation of DS1

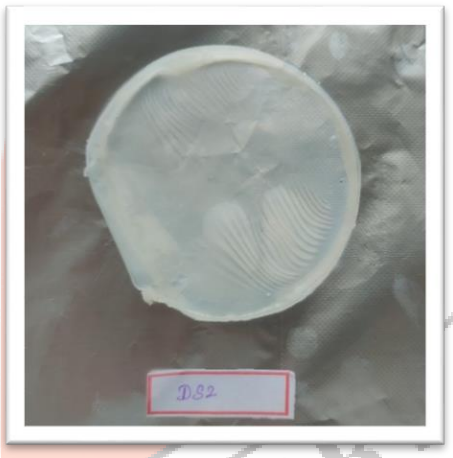

Fig 5: Formulation of DS2

Fig 6: Formulation of DS3

Fig 7: Formulation of DN1

Fig 8: Formulation of DN2

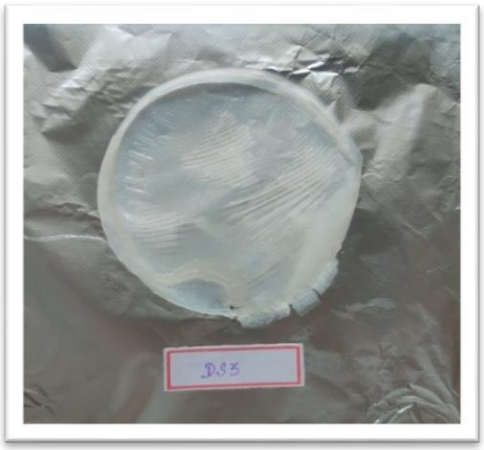

Fig 9: Formulation of DN3

WEIGHT VARIATION

Table No: 4 Weight Variation of MDF of Domperidone

Srno	Formulationcode	Weight in mg ±S.D. n=3
1	DS1	195.1±0.3602
2	DS2	204.5±0.135
3	DS3	207.2±0.2278
4	DN1	202.4±0.1374
5	DN2	204.3±0.1434
6	DN3	206.2±0.0760

THICKNESS

Table No: 5 Thickness of MDF of Domperidone

Sr no	Formulation code	Thickness inmm ± S.D.n=3
1	DS1	0.8±0.5
2	DS2	0.9±0.4
3	DS3	1.2±0.7
4	DN1	0.8±0.7
5	DN2	0.9±0.6
6	DN3	0.8±0.5

FOLDING ENDURANCE

Table No: 6 Folding Endurance of MDF of Domperidone

S. NO	Formulation code	Folding Endurance
1	DS1	>360
2	DS2	>360
3	DS3	>360
4	DN1	>360
5	DN2	>360
6	DN3	>360

CONTENT UNIFORMITY

Table No: 7 Content Uniformity of MDF of Domperidone

Sr no	Formulation code	Percentage of Drug ± S.D. n=3
1	DS1	100.4±3.52
2	DS2	104.6±2.74
3	DS3	102.55±0.4713
4	DN1	96.55±4.25
5	DN2	98.75±1.07
6	DN3	100.6±3.1327

SURFACE pH

Table No: 8 Surface pH of MDF of Domperidone

Sr no	Formulation code	Surface pH ± S.D. n=3
1	DS1	6.1±0.10
2	DS2	6.7±0.20
3	DS3	6.3±0.10
4	DN1	7.6±0.10
5	DN2	7.5±0.32
6	DN3	7.5±0.25

DISINTEGRATION TIME

Table No: 9 Disintegration time of MDF of Domperidone

Sr no	Formulation code	Disintegration Time ± S.D. n=3
1	DS1	75.0±1.41
2	DS2	73.7±2.94
3	DS3	64.4±2.08
4	DN1	45.3±2.65
5	DN2	38.0±2.00
6	DN3	51.7±2.94

% CUMULATIVE DRUG RELEASE FROM DS1, DS2, DS3, DN1, DN2, DN3

Table No: 10 *In vitro* Drug release study of MDF of Domperidone

TIME (Sec)	% CUMULATIVE DRUG RELEASE					
	DS1	DS2	DS3	DN1	DN2	DN3
1	27.4	29.7	19.30	23.4	28.6	24.2
2	52.6	52.7	48.50	57.6	64.2	58.4
3	61.2	61.2	59.40	68.4	76.4	66.6
4	75.6	72.8	77.20	81.2	87.3	84.4
5	82.4	84.6	86.90	91.3	96.8	92.3

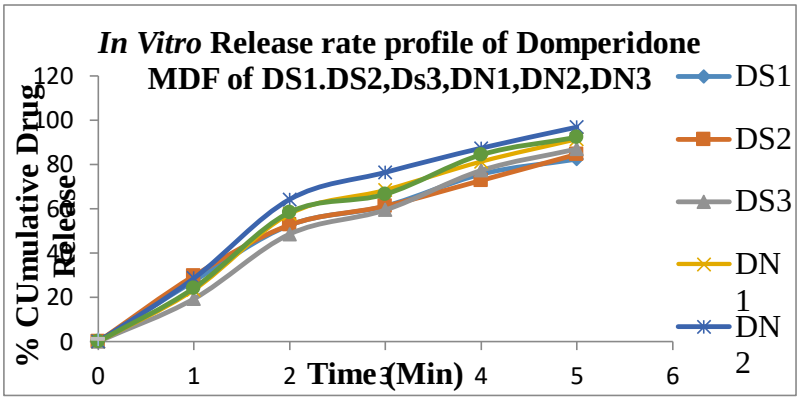

Fig 10: Formulation of DN3

The morphology of all the formulations was found smooth and transparent except DS3.This formula contains highest amount of PVA having air bubble.

The folding endurance for all the formulation was found more than 360 times which was satisfactory to reveal good film properties for all the formulation. The results were depicted in Table No 6.

The drug content uniformity of formulations varied between 97.85% to 105.4%. This is within the desirable range. The observed results of content uniformity indicate that the drug is uniformly distributed throughout the film. The results were depicted in Table No 7.

Weight of the films was found to be in the range of 185.1 mg to 210.2 mg. As the proportion of the polymers is increasing, correspondingly the weight of film is increasing. The results were depicted in Table No 4.

The Thickness for all the formulation was found between 0.8-.1.2mm which was good to film properties. The results were depicted in Table No 5.

In vitro drug release studies were performed for all the prepared formulation by using phosphate buffer pH 6.8 as a dissolution medium and measuring drug concentration by UV-VISIBLE spectrometer at 285.0 nm. The studies were performed up to 2 min. The results of in vitro studies are shown in the Table No 10. Distinguishable difference was observed in the release of Domperidone containing various concentrations of Synthetic and Natural Polymer. The graph was plotted by taking Cumulative Percent Release (CPR) vs. Time and the graphs.

SUMMARY AND CONCLUSION

The present study revealed that the MDFs of Domperidone could be successfully prepared by solvent casting technique with the intention of obtaining better therapeutic efficiency with increasing bioavailability and improving patient compliance. Formulation DN2 SA released 98.9% of drug within 10 minutes and was considered as the best formulation. As the concentration of film forming polymers gets increased it also increases the film forming capacity of the films. From above discussion, it can be concluded that the successful formation and optimization of fast dissolving films of Domperidone using Natural Polymer as film forming polymer and PEG-400 as a plasticizer Hence Domperidone can be conveniently administered orally in the form of films.

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