INTERNATIONAL JOURNAL OF PHARMACEUTICAL RESEARCH AND NOVEL SCIENCES

IJPRNS

FORMULATION DEVELOPMENT AND EVALUATION OF PROCHLORPERAZINE ORAL FAST DISSOLVING FILMS

M.S.Rani*, K.S.H.Priyanka, D.Anusha, G.Srivani, K.Uttara Sailu, K.Ganesh

Department of Pharmaceutics, JITS College of Pharmacy, Kalgampudi, Andhra Pradesh, India.

ABSTRACT

The main objective of the study was to formulate and evaluate oral thin film containing Prochlorperazine. The 5 and 2 % w/v HPMC, PG, CCS films were prepared by solvent casting method. Compatibility of Prochlorperazine with polymers was confirmed by FT-IR studies. films were evaluated for weight variation and thickness showed satisfactory results. Tensile strength and folding endurance of the films were increased with increase in the concentration of polymer due to increase in the elasticity nature of the polymer. Mouth dissolving time and disintegration time of the films were increased with increase in the concentration of the polymer, as more fluid is required to wet the film in the mouth. The presence of disintegrant showed a considerable effect on the disintegration time of the films. Content uniformity study showed that the drug is uniformly distributed in the film. No differences were observed in *invitro* dissolution of drug from the formulated film p1-p9 as the film instantly gets wet by dissolution medium. Present study reveals that all the formulated films showed satisfactory film parameters. It can be concluded that, Oral thin film-containing Prochlorperazinecan be prepared by solvent casting method. 5% w/v of HPMC (FV) film exhibited required tensile strength, folding endurance and disintegration time. The drug release was about 98.6 % in 300 seconds.The accelerated stability studies of the optimized P8 formulation indicates that the formulated oral thin films were unaffected after 3 months storage under accelerated conditions as there were no signs of visually distinguishable changes in appearance, disintegration time and cumulative percentage of drug release. From the present investigation it can be concluded that oral thin film formulation can be a potential novel drug dosage form for pediatric, geriatric and also for general population.

KEY WORDS: Prochlorperazine, oral thin film, HPMC, PG, CCS films

Author for correspondence
M.S.Rani,
Department of Pharmaceutics,
JITS College of Pharmacy, Kalgampudi,
Andhra Pradesh, India.
Email id: sureshbabu3377@gmail.com

INTRODUCTION

Oral route is most preferred route by medical practitioners and manufacturer due to highest acceptability of patients. About 60% of all dosage forms available are the oral solid dosage form. The lower bioavailability, long onset time and dysphagia patients turned the manufacturer to the parenterals and liquid orals. But the liquid orals (syrup, suspension, emulsion etc) have the problem of accurate dosing mainly and parenterals are painful drug delivery, so most patient incompliance. Each pharmaceutical

company wants to formulate the novel oral dosage form which has the higher bioavailability, quick action and most patient compliance. So they formulate the fast dissolving tablets by using super disintigrant/s and hydrophilic ingredients. Fast dissolving drug delivery systems were first developed in the late 1970s as an alternative to conventional dosage forms for pediatric and geriatric patients who experience difficulties in swallowing traditional oral solid-dosage forms. Systemic drug delivery through the sublingual route had emerged from the desire to provide immediate onset of pharmacological effect. Dysphagia (difficulty in swallowing) is a common problem of all age groups, especially elderly, children, and patients who are mentally retarted, uncooperative, nauseated or on reduced liquid- intake/diets have difficulties in swallowing these dosage forms. Sublingual administration of the drug means placement of the drug under the tongue and drug reaches directly in to the blood stream through the ventral surface of the tongue and floor of the mouth. The 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 then drained in to systemic circulation. 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. For these formulations, the small volume of saliva is usually sufficient to result in tablet disintegration in the oral cavity. Sublingual absorption is mostly rapid in action, but also short acting in duration. Nitroglycerine, for example, is an effective anti anginal drug but is extensively metabolized when taken orally (>90%). It is rapidly absorbed through the sublingual mucosa, and its peak plasma level is reached within 1-2 min. Because of its short biological half life (3-5 min.), however the blood concentration of nitroglycerine declines rapidly to a level below the therapeutic concentration within 10-15 min (1-4). In terms of permeability, the sublingual area of the oral cavity is more permeable than the buccal (cheek) area, which in turn is more permeable than the palatal (roof of the mouth) area. The differences in permeability are generally based on the relative thickness, the blood supply, and degree of keratinization of these membranes. In addition to the differences in the permeability of the various mucous membranes, the extent of drug delivery is also affected by the physicochemical properties of the drug to be delivered. Sublingual products have been developed for numerous indications ranging from migraines (for which rapid onset of action is important) to mental illness (for which patient compliance is important for treating chronic indications such as depression and schizophrenia) (5).
The aim of the present investigation is to design, formulate and evaluate the oral disintegrating films taking Prochlorperazine as a model drug to improve the bioavailability and providing faster onset of action to relieve immediately acute migraine attack.

MATERIALS AND METHODS

Preparation of Oral thin film (6, 7)

Film was prepared by using specified polymer by solvent casting method. The specified amount of polymer was weighed and dissolved in specified amount of water for overnight to get a uniform dispersion of 2.5 %, 5% and 7.5 % (w/v) solution respectively. Drug, HPMC, aspartame, citric acid were dissolved in specific amount of water in a beaker. The drug solution was added to the polymer solution and mixed using magnetic stirrer for 1 hour (Table-1). The resulting solution was degassed so as to remove any bubbles formed. The bubble free solution was casted on to a petri dish of surface area 28.6 cm^2. It was dried for 24 hours at room temperature. The film was removed from the petri dish very carefully and observed for any imperfections. Film that was clear and bubble free was selected for further studies. Film of area 2.25 cm^2 (1.25 X 1.25) was cut and stored in a butter paper coved with aluminum foil and stored in a desiccator.

Table-1 Composition of various oral thin film formulations

S no	Ingredients (mg/film)	P1	P2	P3	P4	P5	P6	P7	P8	P9
1	Prochlorperazine	5	5	5	5	5	5	5	5	5
2	CMC*	2.5	5	7.5	-	-	-	-	-	-
3	PVA*	-	-		2.5	5	7.5	-	-	-
4	HPMC* (15cps)	-	-	-	-	-	-	2.5	5	7.5
6	CCS	2	2	2	2	2	2	2	2	2
7	PG**	20	20	20	20	20	20	20	20	20
8	Aspartame	1	1	1	1	1	1	1	1	1
9	Sodium saccharine	1	1	1	1	1	1	1	1	1
10	Water	Qs	qs	qs	qs	qs	qs	qs	qs	qs
	Total Weight[mg]	31.5	34	36.5	31.5	34	36.5	31.5	34	36.5

In vitro Dissolution studies

Dissolution study was carried out using USP type I (basket apparatus) with 500 ml of 6.8 pH Phosphate buffer as dissolution medium maintained at 37 $\pm 0.5^0$ C. Medium was stirred at 50 rpm for a period of 30 minutes. Samples were withdrawn at every 2 min interval up to 30 min, replacing the same amount with the fresh medium. Samples were suitable diluted with 6.8 pH and analyzed for drug content at 258 nm.

RESULTS AND DISCUSSION

Oral thin films containing Prochlorperazine were prepared by casting method. The films of HPMC, CMC and PVA (low viscosity) were prepared with an objective to dissolve the film in the mouth. 2.5%, 5% and 7.5 % w/v each of HPMC, CMC and PVA films were exhibited desired mouth dissolving time and other film parameters, compared to 2.5%, 5% and 7.5 % of HPMC, CMC and PVA films which were difficult to remove and having low strength and exhibited unacceptable mouth dissolving time. Hence 2.5%, 5% and 7.5 % w/v of HPMC, CMC and PVA films were used for the study (Fig 1-4). Propylene glycol (20 % w/w of polymer) was used as plasticizer and to enhance the tensile strength of film.2 % cross carmellose sodium is used as disintegrant to dissolve the films rapidly when comes in contact with saliva. 1 % w/w Sodium saccharine was used as a sweetener and 1 % w/w of aspartame was used as flavoring agent.

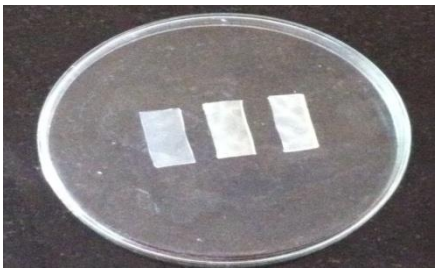

Fig-1: Oral thin film of HPMC

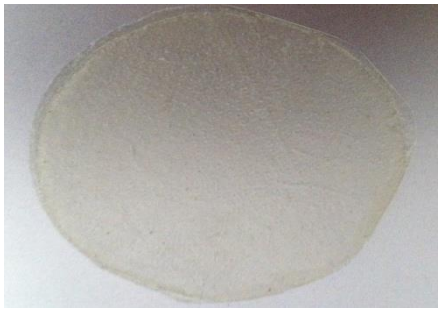

Fig-2 Oral thin film of Hydroxy propyl methyl cellulose

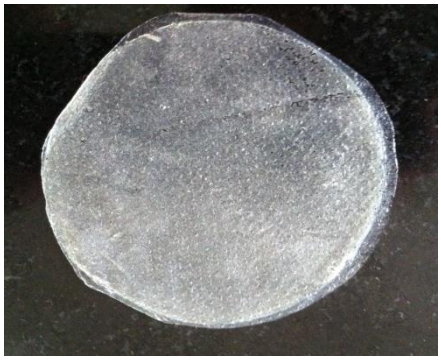

Fig-3 Oral thin film of Carboxy methyl cellulose

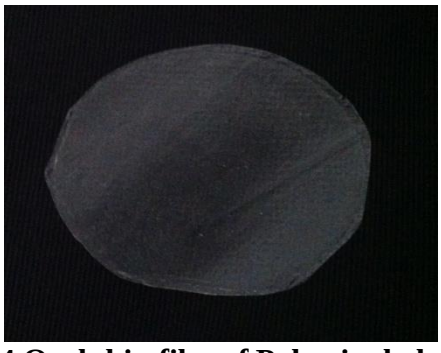

Fig-4 Oral thin film of Poly vinyl alcohol

The disintegration time of the film was done by using tablet disintegration test apparatus. Disintegration times of the films were found to be increased with increase in the concentration of the polymer. The formulation FV shows 32 Sec (disintegration time) as shown in the table-2.

Table-2 Comparative evaluation of Disintegration time of oral thin films

S.NO	Formulation code	Disintegration time in Sec			Mean ± SD*
		Trial 1	Trial 2	Trial 3	
1	P1	46	44	46	45 ± 2
2	P2	48	52	51	50 ± 2
3	P3	40	38	43	40± 1
4	P4	41	44	40	41.6 ± 1.5
5	P5	36	38	35	36.3 ± 1.5
6	P6	45	46	42	44.3 ± 1.2
7	P7	38	40	41	39.6 ± 1.1
8	P8	32	30	34	32 ± 1
9	P9	40	45	42	42.3 ± 1.5

The mouth dissolving time was determined by using beaker containing 6.8-pH phosphate buffer. A size of 0.35 square inch film was subjected for this study. The mouth dissolving time of the film was reported in the Table-3.

Table-3 Comparative evaluation of Mouth dissolving time of oral thin films

S.NO	Formulation code	Mouth dissolving time in Sec			Mean ± SD*
		Trial 1	Trial 2	Trial 3	
1	P1	44	45	42	43.6 ± 1.52
2	P2	54	57	51	54 ± 3.05
3	P3	42	44	43	43 ± 2
4	P4	54	56	58	56 ± 2.05
5	P5	42	46	44	44 ± 2.04
6	P6	47	52	54	51± 2.21
7	P7	60	62	62	61.3 ± 1.05
8	P8	40	38	40	39.3 ± 2.04
9	P9	48	50	52	50 ± 2.05

The dissolution study was carried out using USP Type I (Basket type) dissolution apparatus. The dissolution was carried out in 500 ml of pH 6.8 phosphate buffer maintained at 37 ± 0.5^0C at 50 rpm. 5 ml aliquots of samples were taken at various time intervals which were replaced with same volume of fresh pH 6.8 phosphate buffer maintained at 37 ± 0.5^0C. Prochlorperazine in the samples was then determined spectrophotometrically at λmax of 258 nm. The results were expressed in table-4.

Table-4 Comparative evaluation of *Invitro* dissolution profiles of oral thin Films

Time in min	Cumulative % of drug release								
	P1	P2	P3	P4	P5	P6	P7	P8	P9
2	25	22.6	22	21	26.9	30	32.8	41	34

4	52.3	46.9	44.3	39.8	38.7	52.1	47.1	73.7	47.6
6	76.3	70	62	56	52.54	69.3	58.2	88.4	64.2
8	90.2	84.3	80	71.4	64.5	77.5	68.4	98.6	79.2
10	93.3	92	92.4	82.7	74.2	86.8	79.2	98.6	84.2
12	94.2	93.4	94.5	90.1	86.4	91.8	92.6	98.6	90.3
14	95.4	94.3	97	96.3	98.3	96.8	97.4	98.6	97.29
16	97.2	95.8	97.4	97	98.3	96.8	97.4	98.6	97.29
18	97.2	96.4	97	97	98.3	96.8	97.4	98.6	97.29
20	97.2	97.4	97	97	98.3	96.8	97.4	98.6	97.9

CONCLUSION

Compatibility of Prochlorperazine with polymers was confirmed by FT-IR studies. films were evaluated for weight variation and thickness showed satisfactory results. Tensile strength and folding endurance of the films were increased with increase in the concentration of polymer due to increase in the elasticity nature of the polymer. Mouth dissolving time and disintegration time of the films were increased with increase in the concentration of the polymer, as more fluid is required to wet the film in the mouth. The presence of disintegrant showed a considerable effect on the disintegration time of the films. Content uniformity study showed that the drug is uniformly distributed in the film. No differences were observed in *invitro* dissolution of drug from the formulated film p1-p9 as the film instantly gets wet by dissolution medium. Present study reveals that all the formulated films showed satisfactory film parameters. It can be concluded that, Oral thin film-containing Prochlorperazinecan be prepared by solvent casting method. 5% w/v of HPMC (FV) film exhibited required tensile strength, folding endurance and disintegration time. The drug release was about 98.6 % in 300 seconds. The accelerated stability studies of the optimized P8 formulation indicates that the formulated oral thin films were unaffected after 3 months storage under accelerated conditions as there were no signs of visually distinguishable changes in appearance, disintegration time and cumulative percentage of drug release. From the present investigation it can be concluded that oral thin film formulation can be a potential novel drug dosage form for pediatric, geriatric and also for general population.

REFERENCES

1. Ishikawa T, Koizumi N, Mukai B. Pharmacokinetics of acetaminophen from rapidly disintegrating compressed tablet prepared using microcrystalline cellulose (PHM06) and spherical sugar granules. *Chem Pharm Bull* (Tokyo) 2001; 49: 230-32.
2. Price TM, Blauer KL, Hansen M, Stanczyk F, Lobo R, Bates GW. Singledose pharmacokinetics of sublingual versus oral administration of micronized 17 beta estradiol. *Obstet Gynecol* 1997; 89: 34045.
3. R.P Walton *Absorption of drugs through the oral mucosa. III Fat water solubility coefficient of alkaloids*. Proc Soc Exp Bio Med 1935; 32: 1488.
4. Kurosaki Y, Takatori T, Nishimura H, Nakayama T, Kimura T . Regional variation in oral mucosal drug absorption permeability and degree of keratinization in hamster oral cavity. *Pharm Res* 1991; 8: 1297-1301.
5. Ghosh TK, Chatterjee DJ, Pfister WR. *Quick dissolving oral dosage forms: Scientific and regulatory considerations from a clinical pharmacology and biopharmaceutical perspective*. In: Ghosh TK and Pfister WR (Eds). Drug Delivery to the Oral Cavity Molecules to Market. NY, USA: CRC Press, 2005: 337-356.
6. Bhyan Bhupinder , Jangra Sarita, "Formulation and evaluation of fast dissolving sublingual films of Rizatriptan Benzoate", *International Journal of Drug Development & Research* 2012, 4, 975-979.
7. Han HJ, Floros DJ, Casting antimicrobial packaging films and measuring their physical properties and antimicrobial activity. *J. Plastic Film and Sheeting*. 2010; 18, 287-298

ISSN: 2395-0536 Impact Factor- 2.95*