Research Article

OPTIMIZATION OF FORMULATION OF FAST DISSOLVING FILMS MADE OF PULLULAN POLYMER

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ABSTRACT

This aim of the present study was to optimize the formulation of fast dissolving films made of pullulan polymer. The films formed from solvent casting method and subsequent evaporation of solvent resulted in pullulan forming a circular film. Pullulan was used as film forming agent due to excellent film forming property. PEG, propylene glycol, glycerine were used as plasticizers. Increasing pullulan concentration in formulation resulted in thick films as compared to lower concentration of same. Thickness of the film was controlled by adjusting the concentration of polymer. Higher concentration of polymer and plasticizer results in increase in-vitro disintegration time and in-vitro dissolution time of films. PEG forms white colored films i.e. translucent films. Films containing glycerin takes longer time to dry than films containing propylene glycol. Lower concentration of pullulan and propylene glycol showed optimum performances.

Keywords: Fast dissolving films, Pullulan, Solvent casting, PEG, Propylene glycol, Glycerine, In-vitro disintegration time, In-vitro dissolution time.

INTRODUCTION

Recent developments in the technology have presented viable dosage alternatives from oral route for pediatrics, geriatric, bedridden, nauseous or noncompliant patients. Pharmaceutical companies and consumers alike have embraced OTFs as a practical and accepted alternative to traditional OTC medicine forms such as liquids, tablets, and capsules.[1, 2]

OTFs are typically the size of a postage stamp and disintegrate on a patient's tongue in a matter of seconds for the rapid release of one or more APIs.[3] The use of film-forming polymers in dissolvable films has attracted considerable attention in medical and nutraceutical applications.[4]

In the recent study work has been reported for fast dissolve oral-films that employ pullulan polymer and various plasticizers. Optimization of concentration of polymer and plasticizer has been reported. Pullulan is a water soluble, neutral linear polysaccharide consisting of α–1, 6-linked maltotriose residues. It is a fungal exopolysaccharide produced from starch by Aureobasidium pullulans.[5]

MATERIALS AND METHODS

Materials

Pullulan (water soluble polymer) was obtained from Hayashibra Co., Ltd, Okayama, Japan. PEG 300 (plasticizer) was obtained from SD Fine Chem. Ltd, Mumbai. PEG 400 (plasticizer) was obtained from Thermo fisher scientific India Pvt. Ltd, Mumbai. Propylene glycol (plasticizer) was obtained from Merck Specialties Pvt Ltd, Ambernath. Purified water was used as a solvent. All ingredients were of analytical grade.

Methods

Film formation

Films were formed using solvent-casting method. Different concentration solutions of Pullulan polymer were prepared. And then required amount of plasticizer (PEG300, PEG400, Propylene glycol, glycerin) was added if required. Solutions were kept in sonicator to remove air bubbles. Then the solutions were transferred to Petri plates in duplicate in equal amounts. Petri plates were kept in oven at desired temperature to dry the films. When dried, the films were cut into strips of required size (2x3 cm) and evaluated for thickness, in-vitro disintegration time and in-vitro dissolution time.[6]

Thickness was measured using screw gauze. In-vitro disintegration time and in-vitro dissolution time of strips was determined visually in glass dish of 25ml distilled water with swirling every 10sec. Disintegration time is the time when the strip starts to break or disintegrates. Dissolution time is the time when the strip completely dissolves.[7]

Table 1, 2 shows formulation of various batches of films SG(131)001,005,012,017,022. 5-25% w/w solution of pullulan forms flexible films.[8] Plasticizers are used in concentration of 0-20% w/w of dry polymer weight.[9, 10]

RESULTS AND DISCUSSION

Films formed were transparent, clear, shiny, homogenous and smooth.

Typical strips or films will be between 10-50 mm wide, and 10-50 mm long and weigh 20-100 mg.[11]

Maximum dissolution time for fast dissolving films is 60sec and thickness 20-70µm.[12]

Films formed of pullulan and with plasticizer were transparent except formed with PEG as films formed were translucent i.e. white colored films. PEG reacts with pullulan forming white precipitates.

Table 3 shows the evaluation parameters of marketed strip Listerine.

Table 4, 5, 6, 7, 8 compares the evaluation parameters of various batches SG (131)001, 005,012,017,022.

Table 1: Formulation of films of batch no. SG (131)001, SG(131)005

BATCH NO.	CONCENTRATION OF POLYMER	PULLULAN		PURIFIED WATER	
		Qty/Plate (gm)	Qty/Batch (gm)	Qty/Plate (ml)	Qty/Batch (ml)
SG(131)001	5%	0.480	2.500	9.520	50
	10%	0.910	5.000	9.090	50
	15%	1.300	7.500	8.700	50
	20%	1.670	10.000	8.330	50
	25%	2.000	12.500	8.000	50
SG(131)005	2%	0.196	0.500	9.804	25
	2.5%	0.244	0.625	9.756	25
	5%	0.476	1.250	9.524	25
	7.5%	0.698	1.875	9.302	25
	10%	0.909	2.500	9.091	25

Table 2: Formulation of films of batch no. SG (131)012, SG (131)017, SG(131)022

BATCH NO	CONCENTRATION OF POLYMER & PLASTICIZER	PULLULAN		PURIFIED WATER		PLASTICIZER	
		Qty/Plate (gm)	Qty/Batch (gm)	Qty/Plate (ml)	Qty/Batch (ml)	Qty/Plate (gm)	Qty/Batch (gm)
SG(131)012	2.5%+10%PEG300	0.244	0.625	9.756	25	0.024	0.06
	2.5%+20%PEG300	0.244	0.625	9.756	25	0.048	0.12
	2.5%+10%PEG400	0.244	0.625	9.756	25	0.024	0.06
	2.5%+20%PEG400	0.244	0.625	9.756	25	0.048	0.12
	5% + 10% PEG300	0.476	1.250	9.524	25	0.048	0.12
	5% + 20% PEG300	0.476	1.250	9.524	25	0.096	0.24
	5% +10% PEG400	0.476	1.250	9.524	25	0.048	0.12
	5% + 20% PEG400	0.476	1.250	9.524	25	0.096	0.24
SG(131)017	2.5% + 2.5% PG	0.49	1.25	19.51	50	0.0123	0.0308
	2.5% + 5% PG	0.49	1.25	19.51	50	0.0245	0.0613
	2.5% + 10% PG	0.49	1.25	19.51	50	0.0490	0.1225
	2.5% + 15% PG	0.49	1.25	19.51	50	0.0735	0.1838
	2.5% + 20% PG	0.49	1.25	19.51	50	0.0980	0.2450
	5% + 2.5% PG	0.95	2.50	19.05	50	0.0238	0.0595
	5% + 5% PG	0.95	2.50	19.05	50	0.0475	0.1188
	5% + 10% PG	0.95	2.50	19.05	50	0.0950	0.2375
	5% + 15% PG	0.95	2.50	19.05	50	0.1425	0.3563
	5% + 20% PG	0.95	2.50	19.05	50	0.1900	0.4750
SG(131)022	2.5% + 2.5% GLY	0.49	1.25	19.51	50	0.0123	0.0308
	2.5% + 5% GLY	0.49	1.25	19.51	50	0.0245	0.0613
	2.5% + 10% GLY	0.49	1.25	19.51	50	0.0490	0.1225
	2.5% + 15% GLY	0.49	1.25	19.51	50	0.0735	0.1838
	2.5% + 20% GLY	0.49	1.25	19.51	50	0.0980	0.2450
	5% + 2.5% GLY	0.95	2.50	19.05	50	0.0238	0.0595
	5% + 5% GLY	0.95	2.50	19.05	50	0.0475	0.1188
	5% +10% GLY	0.95	2.50	19.05	50	0.0950	0.2375
	5% + 15% GLY	0.95	2.50	19.05	50	0.1425	0.1425
	5% + 20% GLY	0.95	2.50	19.05	50	0.190	0.1900

Table 3: Evaluation parameters of marketed strips (LISTERINE)

WEIGHT (g)	THICKNESS (mm)	IN-VITRO DISINTEGRATION TIME (sec)	IN-VITRO DISSOLUTION TIME (sec)
0.0331	0.05, 0.05, 0.05	3	35

Table 4: Optimization of Pullulan polymer concentration using strips of 2cm×3cm size of batch no. SG(131)001

PARAMETERS: 10ml solution in Petri plates, Temp.: 40°C-45°C, Drying time- 44hrs				
Pullulan concentration	**Weight (g)**	**Thickness (mm)**	***In-vitro* disintegration time (sec)**	***In-vitro* dissolution time (sec)**
5%	0.0247	0.05,0.05,0.06	5	35
10%	0.0567	0.07, 0.07,0.06	16	60
15%	0.1013	0.12, 0.12,0.11	35	85
20%	0.1306	0.17, 0.17,0.18	67	160
25%	0.1813	0.20, 0.20,0.23	120	257
CONCLUSION: Films formed with lower concentration of polymer (5%, 10%) showed optimum results.				

Table 5: Optimization of Pullulan polymer concentration using strips of 2cm×3cm size of batch no. SG(131)005

PARAMETERS: 10ml solution in Petri plates, Temp.: 40°C-45°C, Drying time- 44hrs				
Pullulan concentration	**Weight (g)**	**Thickness (mm)**	***In-vitro* disintegration time (sec)**	***In-vitro* dissolution time (sec)**
2%	0.0153	0.04, 0.04,0.04	2	25
2.5%	0.0262	0.05, 0.05,0.04	3	30
5%	0.0330	0.06, 0.06,0.05	5	38
7.5%	0.0420	0.07, 0.07,0.08	7	42
10%	0.0550	0.07, 0.08,0.08	11	60
CONCLUSION: Films formed with lower concentration of polymer (5%, 10%) showed optimum results.				

Table 6: Optimization of plasticizer (PEG) concentration using strips of 2cm×3cm size of batch no. SG(131)012

PARAMETERS: 10ml solution in Petri plates, Temp.: 50°C-55°C, Drying time- 30hrs				
Pullulan & plasticizer concentration	**Weight (g)**	**Thickness (mm)**	***In-vitro* disintegration time (sec)**	***In-vitro* dissolution time (sec)**
2.5% + 10% PEG300	0.0259	0.05,0.05,0.06	4	18
2.5% + 20% PEG300	0.0309	0.06,0.07,0.08	5	29
2.5% + 10% PEG400	0.0262	0.06, 0.04,0.05	4	19
2.5% + 20% PEG400	0.0335	0.07, 0.08,0.10	6	33
5% + 10% PEG300	0.0488	0.07, 0.07, 0.08	6	30
5% + 20% PEG300	0.0881	0.11, 0.11, 0.11	20	120
5% + 10% PEG400	0.0516	0.07, 0.08, 0.09	21	140
5% + 20% PEG400	0.1002	0.12, 0.11, 0.11	25	160
CONCLUSION: Films formed were translucent i.e. white colored films.				

Table 7: Optimization of plasticizer (PEG) concentration using strips of 2cm×3cm size of batch no. SG(131)017

PARAMETERS: 20ml solution in Petri plates, Temp.: 50°C-55°C, Drying time- 35hrs				
Pullulan & plasticizer concentration	**Weight (g)**	**Thickness (mm)**	***In-vitro* disintegration time (sec)**	***In-vitro* dissolution time (sec)**
2.5% + 2.5% PG	0.0253	0.04, 0.04,0.04	3	28
2.5% + 5% PG	0.0301	0.06, 0.05,0.05	4	36
2.5% + 10% PG	0.0380	0.05, 0.06,0.06	5	45
2.5% + 15% PG	0.0406	0.06, 0.05,0.07	6	59
2.5% + 20% PG	0.0437	0.07, 0.08,0.07	8	65
5% + 2.5% PG	0.0600	0.08, 0.09,0.10	10	65
5% + 5% PG	0.0653	0.08, 0.11,0.10	12	70
5% + 10% PG	0.0880	0.11, 0.12,0.11	16	80
5% + 15% PG	0.1109	0.13, 0.12,0.11	18	92
5% + 20% PG	0.1334	0.14, 0.12,0.13	21	100
CONCLUSION: Films formed were translucent i.e. white colored films.				

Table 8: Optimization of plasticizer (PEG) concentration using strips of 2cm×3cm size of batch no. SG(131)017

PARAMETERS: 20ml solution in Petri plates, Temp.: 50°C-55°C, Drying time- 38hrs				
Pullulan & plasticizer concentration	**Weight (g)**	**Thickness (mm)**	***In-vitro* disintegration time (sec)**	***In-vitro* dissolution time (sec)**
2.5% + 2.5% GLY	0.0302	0.06, 0.07,0.09	4	36
2.5% + 5% GLY	0.0453	0.05, 0.06,0.07	4	38
2.5% + 10% GLY	0.0490	0.08, 0.07,0.07	8	55
2.5% + 15% GLY	0.0570	0.08, 0.07,0.06	9	65
2.5% + 20% GLY	0.0600	0.06, 0.08,0.12	10	70
5% + 2.5% GLY	0.0585	0.08, 0.08,0.08	10	60
5% + 5% GLY	0.0623	0.09, 0.08,0.08	10	65
5% +10% GLY	0.0700	0.09, 0.10,0.10	13	80
5% + 15% GLY	0.0780	0.11, 0.11,0.10	15	110
5% + 20% GLY	0.0888	0.12, 0.13,0.12	15	124
CONCLUSION: Films containing glycerin as plasticizer takes longer time to dry as compared to propylene glycol films.				

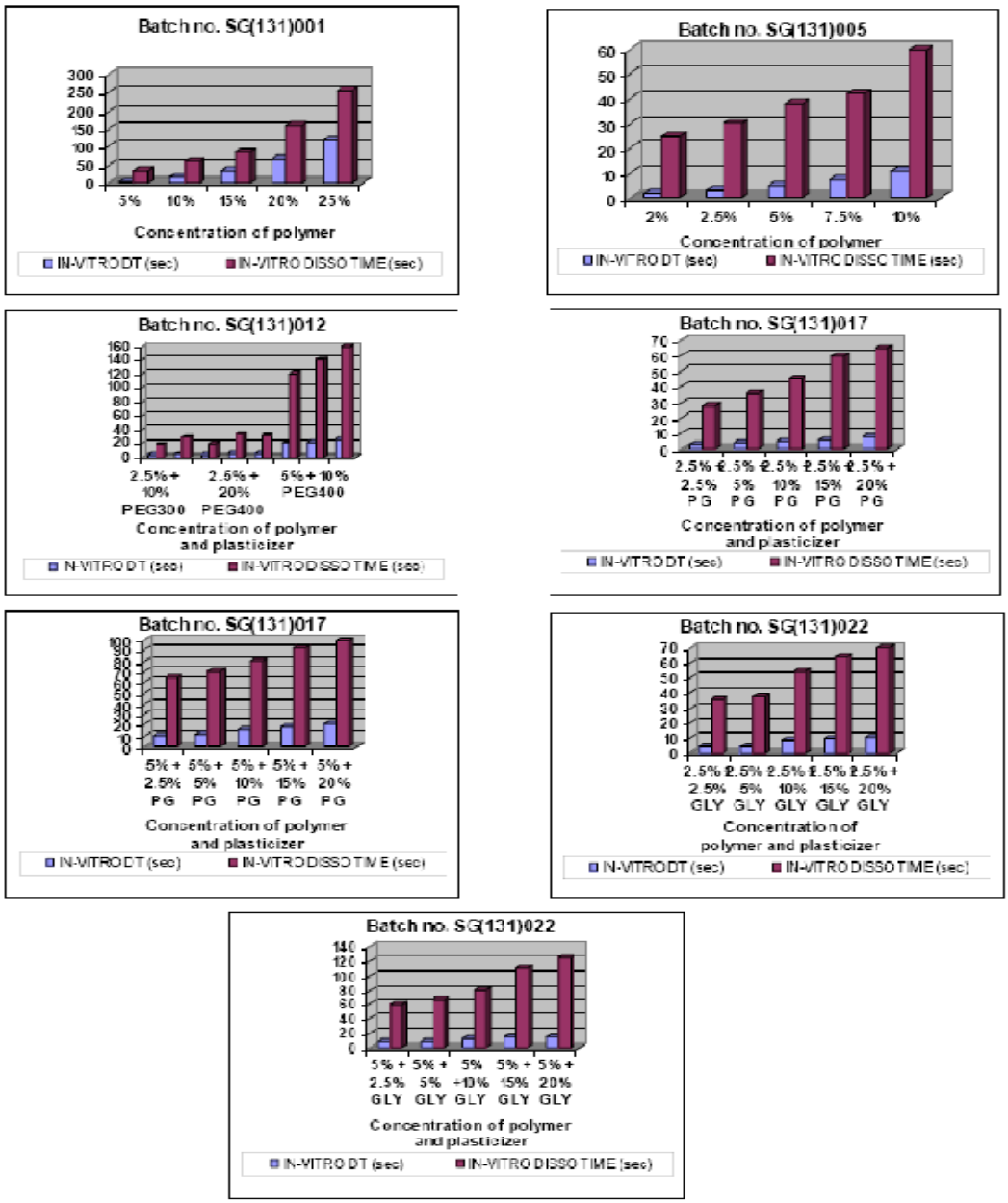

Figure 1: Graphical representation of in-vitro disintegration and dissolution time of all experiments

Weight

By increasing the concentration of pullulan, the weight of strips also increases. Lower concentration is optimum for films.

Thickness

Oral strips should be thin so that they easily dissolve in mouth. It is clear from tables as concentration of polymer increases thickness of films also increases. So lower concentration of polymer was selected for further experiments with plasticizer.

***In-vitro* Disintegration Time and In-vitro Dissolution Time**

Figure 1 graphically represents the in-vitro disintegration and dissolution time of all batches. Higher concentration of polymer and plasticizer results in increase in in-vitro disintegration and dissolution time. Lower concentration of polymer and plasticizer was selected for the formulation of fast dissolving films.

CONCLUSION

The study illustrated that concentration of polymer and plasticizer had a significant effect on formulation of oral strips. Optimization of formulation promoted to determine the influence of concentration of polymer and plasticizer. Circular films were obtained by increasing the amount of solution in Petri plates i.e. 10 ml to 20 ml. Increasing pullulan concentration resulted in formation of thick films as compared to lower one. Lower concentration of polymer and plasticizer showed optimum performances. Propylene glycol shows best results as compared to other plasticizers.

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