Journal of Pharmacreations

PharmaCreations

ISSN: 2348-6295

Pharmacreations \ Vol 9 \ Issue 2 \ Apr - Jun - 20222

Jouranl Home page: www. pharmareations.com

Research article Open Access

Design, Development and Characterization of Oral thin films of Amlodipine besylate,using different polymers, plasticizers and super disintegrants.

Sunil mekala*, Athota Sonia, Chava Alekhya, D.Venkata Pavan, K Bharath Kumar, V.Pravallika

Department of Pharmaceutics, Vishwa bharathi College of Pharmaceutical Sciences, Perecherla, Guntur, Andhra Pradesh, Pin-522601.

Corresponding Author: Sunil Mekala

ABSTRACT

The aim of this study was to prepare pullulanbased orally disintegrating films (ODFs) containing amlodipine besylate, an antihy pertensive drug, by the solvent casting method. For this purpose, nine different ODF formulations (F1F9) were prepared by usin g different plasticizers (glycerol, sorbitol, propylene glycol) and different superdisintegrants (croscarmellose sodium, sodium sta rch glycolate, crospovidone). FD&C Green and aspartame were used as coloring agent and sweetener, respectively. According to the results of preformulation studies, the optimum ODF (F9) was determined and various characterization studies such as unifor mity of mass, film thickness, surface pH of films, and mechanical properties (such as elongation at break, tensile strength, Youn g's modulus, and folding endurance), moisture content, disintegration time, uniformity of content and dissolution test, X.ray, DS C, SEM and short term stability analysis were performed on this formulation.

Keywords: dissolution test, X.ray, DSC, SEM and short term stability analysis etc.

INTRODUCTION

Hypertension

Hypertension is one of the major medical and public health issues. The prevalence of hypertension in children and adolescents appears to be increasing, leading to cardiovascular diseases associated with other disorders. According to public health foundation of India, it is estimated that 20 to 40 percentage population in urban areas and 12 to 17 percentage in rural areas have hypertension. WHO estimated that 33 percentage in men and 32 percentage in women older than 25years have hypertension in India.(1)

The relationship between blood pressure (BP) and risk of cardio vascular disease (CVD) events is continuous, consistent, and independent of other risk factors. The higher the BP, the greater is the chance of heart attack, heart failure, stroke, and kidney disease. Heart disease related mortality increases dramatically with age. Heart disease deaths that occur before the age of 65 are generally considered premature, preventable deaths, and are, therefore, of particular public health significance. Hypertension is one of the main causes of heart disease, and in recent years, the age adjusted hypertension and hypertensive disease death rates are increasing. Consequently, the prevention and treatment of hypertension are of social significance.(2)

Antihypertensive drugs currently available in the market are largely in the form of conventional dosage forms. Due to limitations in the use of conventional dosage forms ,alternative dosage forms such a novel and controlled release products have also been developed. Such products are available in the market for a few drugs. Many antihypertensive drugs are still used in conventional dosage forms.(3) There is a need, therefore, to develop novel drug delivery systems for these categories, so as to optimize the therapy with these drugs. Further, oral thin films are novel drug delivery systems for oral delivery of the drugs. Oral thin films are very thin strips, which release the active ingredient immediately after ruptake into the oral cavity. Films are simply placed on the patient's tongue or any oral mucosal tissue.(4) 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

mucosal absorption or gastrointestinal absorption when allowed.

Oral transmucosal drug delivery

Oral cavity has been considered as a site of absorption for a long period of time Ponchel was found that nitroglycerine was absorbed from the oral cavity in 1993. Since thenvariousactivesubstanceshavebeenstudiedforlocalorsystemicuse.The ability to maintain a delivery system at a particular location for an extended period of time has great appeal for both local as well as systemic drug absorption and it leads to greater bioavailability. Drug absorption through a mucous surface is efficient due to rich in blood supply, and it leads rapid drug transport to the systemic circulation and avoiding degradation by gastrointestinal enzymes and first pass hepatic metabolism.

Due to the excellent accessibility and reasonable patient compliance of oral mucosal cavity, it offers as attractive route for drug administration. Within the oral mucosal cavity, drug delivery is classified into two categories.

i. Sublingual delivery, which is a systemic delivery of drug through the mucosal membrane.
ii. Buccal delivery for the treatment of conditions of the oral cavity. The buccal mucosa however appears well suited to attachment ofretentivedeliverysystem(5)

In human body the oral cavity is the foremost part of digestive system. It is also referred as “buccal cavity”. It is accountable for various primary functions of body. The careful examination of various features of oral cavity can help in development of a suitable buccoadhesive drug delivery system.

MATERIALS AND METHODS

Preparation and optimization of oral thin films of Amlodipine Besylate

In the present investigation, the role of hydrophilic polymers in improving the *in vitro* dissolution rate of a slightly water soluble drugs has been demonstrated. Oral thin films of amlodipine besylate (AML) and polymers in different weight ratios were prepared using solvent evaporation method to study the effect of weight fraction of carrier on the dissolution rate of selected drugs. The differential scanning calorimetry (DSC),(6) and Fourier transform infrared (FTIR) spectroscopy were used to evaluate the drug-polymer interaction in the oral thin films. Saturation solubility studies and *in vitro* dissolution rate studies were also performed to characterize the properties of the films. Drug release kinetics was established by fitting the data into popular kinetic models.(7)

Preparation of oral thin films

The films were prepared by mixing drug, polymer, plasticizer, super disintegrant, aspartame and mango flavour in water. Ultrasonic defoaming apparatus was used to remove the air bubbles in the solution. The mixture was then poured in the petridish to prepare the thin films. The film obtained after drying was cut into 2 cm x 2 cm in size, containing required quantity AML 5mg of the drug. The films were then collected from petridish and stored in a desiccators for further studies.

RESULTS AND DISCUSSIONS

Characterization of the oral thin films: Estimation of drug content

The drug content of all the prepared oral thin films was estimated by the following procedure. The 4cm^2 of the polymeric-drug thin film was placed into a 100 ml volumetric flask. The pH 6.8 phosphate buffer (30ml) was added and the contents were mixed thoroughly to dissolve the drug from the films. The solution was made up to the volume with the same buffer. This solution was filtered through 0.45µm millipore filter. Then the solution was suitably diluted and assayed spectrophotometrically.(8)

Fourier transform infrared Spectroscopy (FTIR)

The FTIR spectrum was obtained on a Perkin Elmer 2000 FTIR System (Perkin–Elmer, Norwalk, CT) using KBr press pellet method. The scanning range was 450-4000 cm^{-1}andtheresolutionwas1cm^1.The FTIR spectrum of pure drugs and their optimized formulations.(9)

Differential Scanning Calorimetry

The DSC thermogramsare obtained by a differential scanning calorimeter (DSC220C, SEIKO, JAPAN) at a heating rate of 10□C/min from 10 to 200□C in the nitrogenatmosphere(3,100

Scanning Electron Microscopy (SEM) Studies

Scanning electron microscopy has been extensively employed to study the morphology and the surface to pography of the films. The morphology and the surface to pography of the selected films were, therefore, examined by the scanning electron microscopy (CARL-ZEISS EVO MA 15)[4]. The samples to be examined were mounted on the SEM sample stub using the double sided sticking tape. The samples mounted were coated with gold (200^{0}A) under reduced pressure (0.001 torr) for 5 min. The gold-coated samples were observed under the SEM with suitable magnification.(11)

X-ray Diffraction studies

The powder X-ray diffraction patterns were recorded on a Philips PW 1140 powder X-ray diffractometer using Ni-filtered,CuKα radiation,avoltageof45kV and acurrentof25 mA[5]. The instrument was operated in the continuous scan mode overa 2ø range of 5 to60□with a chart speed of2□/2cm/2ø.

Solubility measurement

The apparent solubility of the pure drugs and the optimized oral thin films were determined in water at 37°C. Each preparation equivalent to 50 mg of drug was added to 50ml of water in a conical flask with teflon-lined screw caps. Then

the conical flasks were kepton a shaker incubator maintained at 37° 0.5°C for 24 hrs. After shaking, the flasks were kept in an incubator at 37°0.5°Cforequilibration for12hrs.Then solution was filtered through 0.45 µm Millipore filter and the filtrate was assayed spectrophotometrically.

Dissolution rate studies

Dissolution rate studies of pure drugs and their oral thin films were determined in500 ml of pH 6.8 phosphate buffer at 37°C with a stirrer rotation speed of 50 rpm using the USP I dissolution rate test apparatus employing the basket. A 5 ml aliquot of dissolution medium was withdrawn at different time intervals with the pipette containing the prefilter.(11)The samples were filtered through 0.45µm millipore filter. Plasticizers were measured in ml. The samples were suitably diluted and assayed spectrophotometrically. Each test is repeated for three times.

The percent of drug dissolved at various time intervals was calculated and plotted against time. The results are shown in their respective tabular columns.

Evaluation of oral thin films

Percentage elongation and tensile strength

The films were cut into a size of 2cm x 2cm strips. One end of the strip along its length was clamped to the tensile strength testing apparatus and the other end was attached to a movable rod. The movable rod was attached to a pan with the help of a non-stretchable string through a pulley.(12) Weights were carefully added onto the pan and the weight was gradually increased. The elongation of the patch was determined by measuring the distance moved by the pointer (on a graph paper) after the addition of the weight each time. The weights were added, until the film was cut.

Percentage elongation was determined using the formula

%elongation atbreak=L_B-L_O/L_O×100

Where
L_O=Original length of patch,
L_B=length of patchat break when stress is applied.

The tensile strength of the thin film was determined using the formula

Tensile strength=Break force/ab[1+(ΔL/L)

$$\textit{Tensile strength} = \frac{W}{a \times b} \times \frac{l + \Delta l}{l}$$

Where,
a=width(cm),
b=thickness(cm),
l=length of the test patch strip(cm),
Δl= elongation at the break point(cm) and
W =weight required to break the patch(g).

Surface pH

The 4cm^2 film of each formulation was taken and was placed in a petridish containing2ml of water. After complete wetting of the film, the pH at the surface of the film was checked using the pH paper and the pH meter.

Folding Endurance

Folding endurance was determined by repeatedly folding the film (2cm× 2cm) at the same place until it breaks at the place of folding. The number of times the film can be folded at the same place without breaking was the folding endurance value.

Thickness

Precise film thickness measurements were carried out using NIKONDigi Microencoders/screw gauge that are used in motion control systems with optical linear encoder heads with a specially developed MPM300-OEMmotion processing module providing nanometer solution. These encoder/gauge heads were used with the NikonTC-101interpolator-counter with digital read-out. The encoders use a 12 volt direct current (VDC)power supply. Thickness was measured at four corners and in the centre of the selected films.(13)

Determination of Moisture Content

The prepared films were weighed and kept in a vacuum desiccators containing anhydrous silica at room temperature. The patches were weighed repeatedly until they showed a constant weight. Percent moisture content was determined using the formula,(14)

$$\%\text{Moisture Content} = \frac{\text{Initial weight of the film} - \text{Final weight of the film}}{\text{Initial weight of the film}} \times 100$$

Weight Variation Test

The 4cm^2 film was cut at three different places in the cast film. The weight of each strip was taken and then the weight variation was observed.

Disintegration Test

Disintegration refers to the physical process by which a film dissolves into a solution. The2ml of water was placed in a petriplate with a film on the surface of water; the time taken for the disintegration of the film.

Calibration curve of amlodipine besylate

The standard solution of AML was subsequently diluted with Phosphate buffer (pH6.8) or purifies water to obtain a series of dilutions containing 2, 4, 6, 8, 10, 12, 14, 16, 20 2428, 32 and 36 □g of AML in 10 ml solution. The absorbance of these samples was measure dat239nmin spectrophotometer (LabIndiaUV-3000,India) against appropriate solvent blank. All the estimations were done in triplicate and average values are reported.

Table 1: *Invitro* evaluation parameters of amlodipine besylate.

Sr.No.	Batch code	Film Mass (mg)	Thickness (µm)	PH	Folding endurance	% elongation	Tensile strength
1.	AML1	114±1	475±5	7.8±0.2	199±4	10.44±0.13	19.82±0.12
2.	AML2	115±2.5	465±15	7.35±0.25	202±1	10.19±0.06	19.74±0.14
3.	AML3	116±1.5	458±8	7.33±0.2	200.3±0.7	10.33±0.04	19.6±0.17
4.	AML4	115±0	468±2	7.78±0.25	197.3±2.3	10.28±0.10	19.48±0.19
5.	AML5	277±2	110±10	7.55±0.05	56.5±1.5	12.57±0.34	21.39±0.05
6.	AML6	278.5±0.5	110±10	7.5±0.1	56.5±1.5	12.23±0.10	21.48±0.09
7.	AML7	277.5±0.5	116.5±3.5	7.45±0.05	57.5±0.5	12.43±0.12	22.18±0.19
8.	AML8	276±1	116.5±3.5	7.5±0	57.5±0.5	12.65±0.14	21.27±0.07
9.	AML9	293±2	635±5	7.05±0.05	14±1	10.4±0.00	18.29±0.10
10.	AML10	294±1	635±5	6.95±0.05	19±4	10.66±0.05	18.31±0.06
11.	AML11	293±0	631.5±1.5	6.95±0.05	20±3	10.33±0.04	18.22±0.07
12.	AML12	292±1	631.5±1.5	7.05±0.02	15±2	10.69±0.09	18.36±0.23
13.	AML13	134±1	320±10	7.1±0.05	83±3	13.22±0.03	18.16±0.01
14.	AML14	134±1	305±5	7.05±0.15	85.5±0.5	13.26±0.02	18.22±0.04
15.	AML15	133±1	306.5±6.5	6.96±0.06	84.3±0.7	13.82±0.03	18.38±0.20
16.	AML16	133±1	321.5±8.5	7.01±0.01	81.8±1.8	13.72±0.04	18.4±0.17

Variation of mass

During the preparation of the oral films, the film solutions were cast into sheets and then cut into smaller strips of 4cm^2(2cm ×2cm). Oral films were cut from different sheets and the variability between the sheets of the respective polymer was investigated. The HPMC 5cps oral thin films showed the highest variation in mass with an average mass of 293 mg. The film strips of HPMC 3cps exhibited an average mass of 277mg, Sodium CMC 133mg and MC E15 115mg. Thus the mass was either lower or higher than the nominal value which can have consequences on the content uniformity. In conclusion, a homogenous distribution of pure drug and, if possible, prevention of recrystallization of pure drug reduces mass variation and enhance the content uniformity.

Table 2: Average mass of AML films made from different polymers

S.NO.	Batch code	Average film mass(mg)
1	AML_{1-4}	115±0.70
2	AML_{5-8}	277.25±0.90
3	AML_{9-12}	293±0.70
4	AML_{13-16}	133.5±0.5

Film Thickness

The determination of film thickness is the most common method to characterize the produced oral thin films.. The micrometer screw gas method was used to determine the thickness of the AML polymeric or a thin films. The thickness of the films was determined by using the screw gauze. Oral thin films made from HPMC 5cps showed an

average film thickness of 633µm, Sodium CMC313µm, HPMC3cps113µm and MC E15466µm.

Table 3:Average thickness of AML films made from different polymers

S.NO.	Batch code	Average film thickness
1	AML_{1-4}	466.5±6.10
2	AML_{5-8}	113.25±3.25
3	AML_{9-12}	633.25±1.75
4	AML_{13-16}	313.25±7.53

Estimation of pH of the oral film

The pH value was determined by dissolving one oral film in 2ml of distilled water and measuring the pH of the obtained solution. Differences were expected because various polymers were used**.** The pH value of AML polymeric oral films was measured by electrometric pH meter. The HPMC grades show the pH values of HPMC5cps(7) and HPMC 3cps pH (7.5). The film strips of Sodium CMC exhibited an average pH of (7.03) andMCE15 pH(7.56).

Table 4: Average pH of AML films made from different polymers

S.NO.	Batch code	Average pH
1	AML_{1-4}	7.56±0.22
2	AML_{5-8}	7.5±0.03
3	AML_{9-12}	7±0.05
4	AML_{13-16}	7.03±0.05

Folding endurance

Folding endurance was determined by repeatedly folding the film (2cm× 2cm) at the same place until it breaks at the place of folding. The **Fig.7.8** shows an average folding endurance of AML polymeric thin films. The MC E15 oral thin films showed the highest folding endurance with an average of 199.6, the film strips of HPMC 5cps exhibited an average folding endurance of 17.3, Sodium CMC83.5, HPMC3cps 57.1.

Estimation of pH of the oral

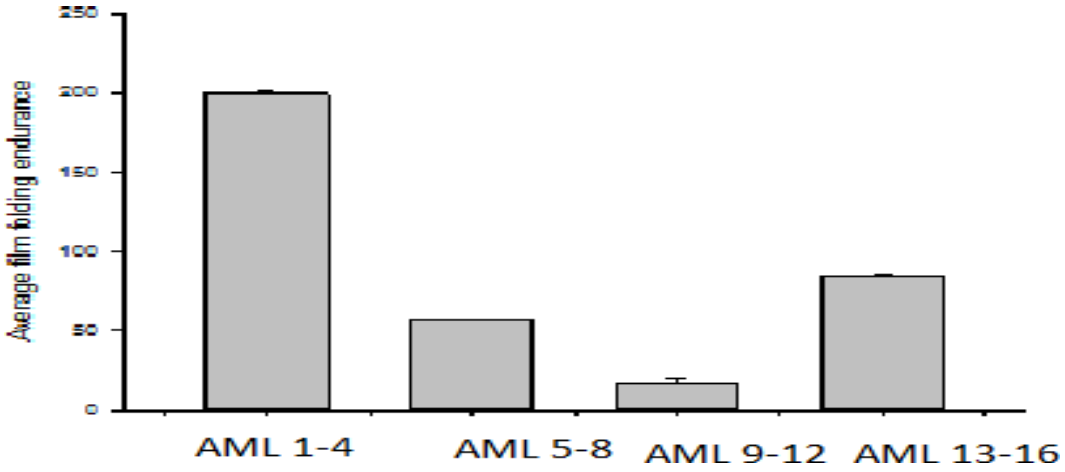

Fig 1: Average folding endurance of AML films made from different polymers

Table 5: Formulae of the prepared oral thin films

Ingredient (mg/film)	AML_1	AML_2	AML_3	AML_4
AML	5	5	5	5
MC-E15	40	40	45	40
SSG	-	5	10	10
CCS	-	-	-	-
Polyplasdone	-	10	5	14.21

XL-10				
Citricacid	5	5	5	5
PEG-400	2	1	1	1
Glycerine	-	-	1	1
Aspartame(mg)	2	2	2	2

Table 6: Comparative dissolution data of AML from pure AML and oral thin films of AML-MC E15 Containing varying concentrations of MC E15

Time(min.)	Pure AML	AML_1	AML_2	AML_3	AML_4
0	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	
1	5.29±1.39	8.5±1.02	8.5±2.39	4.2±0.85	5.4±0.34
3	10.06±1.56	22.3±0.69	15.1±0.02	10.3±0.35	20.2±0.34
5	20.34±2.78	32.1±1.35	24±0.49	15.8±0.35	21.4±0.35
7	34.5±2.3	39.3±2.05	30.4±1.52	20.6±0.53	28±1.89
10	52.6±5.01	48.7±4.98	40.6±3.59	24.9±0.53	41.4±0.37
15	63.37±3.69	61.4±7.94	53.9±2.76	41.1±0.32	71.3±0.72
30	88.2 ±2.4	84.7±9.22	94.8±1.42	97.8±0.19	97.3±3.80
45	-	99.8±7.08	-	-	-

Dissolution rate of AML and its polymeric films were determined in 500 ml of pH 6.8phosphate buffer at 37□C with a stirrer rotation speed of 50 rpm using the USP I dissolution rate test apparatus employing the basket.A5mlaliquotofdissolution medium was withdrawn at different time intervals with the bulb pipette containing the prefilter. The samples were filtered through 0.45µm millipore filter. The samples were suitably diluted and assayed spectrophotometrically (Lab India) at 239 nm. Each test is repeated for three times. The percent drug dissolved at various time intervals was calculated and plotted against time. The films AML_2 and AML_4 showed the slowest drug release at the 3 min time point. compared to the AML pure drug, the filmAML_1showed the drug release 99.8% at the 45mintime point and AML_3 showed the highest drug release 100.9 % at the 30 min time point.

Table 7: Formulae of the prepared oral thin films

Ingredient (mg/film)	AML_5	AML_6	AML_7	AML_8
AML	5	5	5	5
HPMC-3cps	50	50	45	45
SSG	-	10	10	5
CCS	-	-	-	-
Polyplasdone	-	-	5	10
XL-10				
Citricacid	5	5	5	5
PEG-400	2	1	1	1
Glycerine	-	1	1	1
Aspartame(mg)	2	2	2	2

Table 8: Comparative dissolution data of AML from pure AML and oral thin films of AML-HPMC-3cps Containing varying concentrations of HPMC-3cps

Time(min.)	Pure AML	AML_5	AML_6	AML_7	AML_8
0	00.00±0.00	00.00±0.00	00.00±0.00	00.00±0.00	00.00±0.00
1	5.29±1.39	9.9±0.34	7±1.88	11.2±2.39	7.5±1.86
3	10.06±1.56	26.2±0.85	13.7±2.41	18±3.57	15.8±1.73
5	20.34±2.78	37.1±0.51	23.1±0.38	27.3±3.78	23.5±1.6
7	34.5±2.3	45.9±1.7	31±1.24	34.6±3.3	29.2±1.55
10	52.6±5.01	57.8±4.97	41.4±1.43	45.2±3.67	44.2±1.43
15	63.37±3.69	77.4±6.90	60.2±0.93	59.5±2.17	61.4±0.83
30	88.2 ±2.4	104.6±0.15	100.3±5.92	91.8±0.14	100.7±4.92

The percent of drug dissolved at various time intervals was calculated and plotted against time. The films AML_5 ,AML_6 and AML_8 showed the highest drug release at the 30 min time point. When the AML pure drug and AML_7 were compared,

similar drug release was obtained at the 30 min time point.

Table 9:Formulae of prepared oral thin films

Ingredient (mg/film)	**AML_9**	**AML_{10}**	**AML_{11}**	**AML_{12}**
AML	5	5	5	5
HPMC-5cps	45	45	45	45
SSG	-	10	10	10
CCS	-	-	-	--
Polyplasdone	-	-	5	10
XL-10				
Citricacid	5	5	5	5
PEG-400	1	1	1	1
Glycerine	1	1	1	1
Aspartame(mg)	2	2	2	2

Table 10: Comparative dissolution data of AML from pure AMLandoralthinfilmsofAML-HPMC-5cps containing varying concentrations of HPMC-5cps

Time(min)	**Pure AML**	**AML_9**	**AML_{10}**	**AML_{11}**	**AML_{12}**
0	00.00±0.00	00.00±0.00	00.00±0.00	00.00±0.00	00.00±0.0
1	5.29±1.39	7.7±0.86	6.8±0.68	5.1±1.03	5.1±1.37
3	10.06±1.56	18.7±0.52	12.5±0.2	13±0.35	21.9±1.4
5	20.34±2.78	31±1.38	19.3±1.01	19.8±2.24	28.1±0.55
7	34.5±2.3	42.9±8.48	28.4±3.08	27.9±1.57	33±1.06
10	52.6±5.01	56.1±3.34	38.5±2.94	43.9±2.27	47.4±2.1
15	63.37±3.69	73.6±1.80	55.1±4.85	61.3±0.61	61.4±5.37
30	88.2±2.4	102.9±1.5	92.3±1.48	93.8±1.99	99±0.63
45			100.8±2.25		

The percent drug dissolved at various time intervals was calculated and plotted against time. The results are given in **Table 10.** The films $AML_{10}$and AML_{11} showed the slowest drug release at the 30 min time point. When the AML pure drug, AML_9 and AML_{12} were compared, the AML_9 and AML_{12} showed the highest drug release at the30 min time point.

Table 11:Formulae of the prepared oral thin films

Ingredient(mg/film)	**AML_{13}**	**AML_{14}**	**AML_{15}**	**AML_{16}**
AML	5	5	5	5
Sodium CMC	30	30	30	30
SSG	10	10	5	10
CCS	-	-	-	-
PolyplasdoneXL-10	5	10	14.21	14.21
Citric acid	5	5	5	5
PEG-400	1	1	0.5	-
Glycerine	1	0.5	0.5	-
Aspartame(mg)	2	2	2	2

Tbale12: Comparative dissolution profiles of AML from pure AML and oral thin films of AML-sodium CMC Containing varying concentrations of sodium CMC

Time(min.)	**Pure AML**	**AML_{13}**	**AML_{14}**	**AML_{15}**	**AML_{16}**
0	00.00±0.00	00.00±0.00	00.00±0.00	00.00±0.00	00.00±0.00
1	5.29±1.39	7.53±0.00	4.2±2.05	5.1±0.34	2.3±1.03
3	10.06±1.56	13±0.34	11.1±1.73	16.8±0.35	12±0.69
5	20.34±2.78	22.9±0.86	21.5±0.21	28.9±7.54	29.7±1.55
7	34.5±2.3	38.4±4.8	52.5±0.3	51.6±12.23	45.3±1.12
10	52.6±5.01	60.5±6.72	61.7±3.56	83.8±14.59	63.5±2.10
15	63.37±3.69	94±3.41	99.7±0.05	103.6±0.6	82.1±0.94
30	88.2 ±2.4	99.9±1.2	-	-	91.4±1.29

As seen in Table 12the percent of drug dissolved at various time intervals was calculated and plotted against time. The films AML_{13}, AML_{16} and AML pure drug showed the slowest drug release at the 30 min time point. ThefilmsAML_{14}andAML_{15}showedthehighestdrugreleaseatth e15mintimepoint.Inthecase of AML 15 the burst release was observed. The AML_{15} (oral dissolving film with higher amount of super disintegrant Polyplas done XL-10 and SSG) showed fastest onset of drug release. However, it was evident that the oral thin films of AML_{15} with super disintegrant dissolved completely within 15min whereas the oral dissolving films with higher amount ofsuperdisintegrantwithdifferentplasticizersshowedlessamo untofdrugrelease.Inconclusion, the addition of higher amount of super disintegrant to the AML- Sodium CMC(AML_{15})oral dissolving films leads to faster dissolution.

Table 13:Comparison of dissolution data of pure AML, AML15and marketed AML brand

Time(min.)	Pure AML	AML15	Marketed brand
0	00.00±0.00	00.00±0.00	00.00±0.00
1	5.29±1.39	5.1±0.34	5.28±0.01
3	10.06±1.56	16.8±0.35	10.03±0.02
5	20.34±2.78	28.9±7.54	20.32±0.01
7	34.5±2.3	51.6±12.23	34.65±0.15
10	52.6±5.01	83.8±14.59	60.3±0.2
15	63.37±3.69	101.6±0.6	83.5±0.3
30	88.2±2.4	-	89.2±0.1
45	-	-	92.2±0.1

AML release kinetics from polymeric thin films

The values of correlation coefficients (r) and kinetic parameters obtained by fitting the data to the popular drug release models are given in Table 13. The drug release from these formulations appear to follow more of first order kinetics as indicated by r values (0.834-0.998) compared to those of zero order release kinetics (0.800-0.996). When log percent AML remaining was plotted against time, straight lines were obtained for pure AML and polymeric thin film values as shown in the Table 14.

Table 14: Correlation Coefficient (r values) for dissolution data of different oral thin film formulations according to various kinetic models

Product Code	Zero Order	First Order
Pure AML	0.913	0.994
Marketed AML	0.912	0.945
AML_1	0.902	0.998
AML_2	0.987	0.932
AML_3	0.988	0.983
AML_4	0.950	0.950
AML_5	0.969	0.990
AML_6	0.996	0.989
AML_7	0.946	0.994
AML_8	0.994	0.986
AML_9	0.983	0.994
AML_{10}	0.987	0.954
AML_{11}	0.970	0.965
AML_{12}	0.968	0.991
AML_{13}	0.987	0.834
AML_{14}	0.977	0.884
AML_{15}	0.974	0.861
AML_{16}	0.800	0.931

In the last few years, the semi-synthetic hydrophilic polymers have been used as carriers to enhance the dissolution rate and bioavailability of poorly water-soluble drugs. But many of these polymers also limit their application as carriers for dissolution enhancement by their viscosity and toughness. The effect of plasticizer and super disintegrant used in solvent evaporation method one drug release rate was also investigated. Differential Scanning Calorimetry (DSC), and Fourier transform infrared (FTIR) spectroscopy were used to evaluate the drug-carrier interactions in the solid state. Drug release kinetics and mechanism was established by fitting the data in to popular

kinetic models. Our studies have conclusively proved that, synthetic hydrophilic polymers could be used as potential carriers in the dissolution rate enhancement of these drug, AML. The drug release from pure drug and oral thin films followed first order kinetic mechanism. The results demonstrated that optimum AML: Na CMC weight ratio is 1:6. There are no drug carrier interaction sin the oral thin films. Among the various methods used in the preparation of oral thin films, the solvent evaporation technique gave the highest dissolution rate of all the drugs. The characteristics like ease of preparation, reliability in the method, avoidance of the use of organic solvents or high temperatures, make it the most convenient method from a practical point of view. Hence, oral thin films produced by solvent evaporation method were selected for stability studies. The polymer with drug showed good *in vitro* dissolution behavior. These results clearly indicated the influence of the viscosity of polymer and plasticizer in the formulation of OTF. All the *in vitro* evaluation parameters of OTF of drugs were found within the official and fixed limits. From these studies, it can be inferred that scaling up of oral thin film preparation could be useful in finding out a solution to poor success rate of drugs for large scale production. Further, the oral thin film containing amlodipine besylate disintegrates within a minute and hence is potentially useful in managing the hypertension. It is also useful in the case of geriatric patients who show unwillingness to take tablets.

CONCLUSION

In conclusion, our studies showed that, hydrophilic polymers could be used as potential carriers in the dissolution rate enhancement of AML. The AML release from the pure drug and the oral thin films followed first order kinetics. The results demonstrated that the optimum AML: Sodium CMC weight ratio is 1:6. Since, no drug carrier interaction in the oral thin films has been evidenced, increased dispersibility and reduced crystallinity of AML can account for the increased dissolution rate of the films. Oral thin films were prepared by solvent evaporation method. The advantages of the solvent evaporation method are ease of preparation, avoidance of organic solvents or high temperatures. This technique is easy and more convenient and economical from a practical point of view.

REFERENCES

1. Nishimura M, Matsuura K, Tsukioka T, Yamashita H, Inagaki N, SugiyamaT, Itoh Y. In vitro and in vivo characteristics of prochlorperazine oral disintegrating film. Int J Pharm. 2009;368(1-2):98-102. doi: 10.1016/j.ijpharm.2008.10.002, PMID 18992311.
2. Shimoda H, Taniguchi K, Nishimura M, Matsuura K, Tsukioka T, Yamashita H, Inagaki N, Hirano K, Yamamoto M, Kinosada Y, Itoh Y. Preparation of a fast dissolving oral thin film containing dexamethasone: A possible application to antiemesis during cancer therapy. Eur J Pharm Biopharm. 2009;73(3):361-5. doi: 10.1016/j.ejpb.2009.08.010, PMID 19735731.
3. Mishra R, Amin A. Formulation development of taste masked rapidly dissolving films of cetirizine hydrochloride. Pharm TechnolUSA. 2009;33(2):48-56.
4. Chen MJ, Tirol G, Bass C, Corniello CM, Watson G, Sanchez I. Castable edible pharmaceutical films. Drug DelivTechnol. 2008;8(6):34-41.
5. LazarusJ, CooperJ. Absorption, testing, and clinical evaluation of oral prolonged-action drugs.JPharmSci. 1961;50:715-32. doi: 10.1002/jps.2600500902, PMID 13759773.
6. WagnerJG. Interpretation of percent dissolved-time plots derived from in vitro testing of conventional tablets and capsules.JPharmSci. 1969;58(10):1253-7. doi: 10.1002/jps.2600581021, PMID 5349114.
7. WagnerJG.Drug Stand. 1959;27:178.
8. Khan TA, Peh KK, Ching HS. Mechanical, bioadhesive strength and biological evaluation of chitosan films for wound dressing. J.Pharm.. Pharmaceuticals.Sci.2000;3(3):303-11.
9. Fulzele SV, Satturwar PM, Dorle AK. Study of novel rosin based biomaterials for pharmaceutical coating. AAPS PharmSciTech. 2002;3(4):E31. doi: 10.1208/pt030431, PMID 12916925.
10. Koland M, Sandeep VP, Charyulu NR. Fast dissolving sublingual films of ondansetron hydrochloride: effect of additives on *invitro*drug release and mucosal permeation. Journal of Young Pharmacists. 2010;2(3):216-22. doi: 10.4103/0975-1483.66790.
11. Shimoda H, Taniguchi K,Nishimura M, Matsuura K, Tsukioka T, Yamashita H, Inagaki N, Hirano K, Yamamoto M, Kinosada Y, Itoh Y. Preparation of a fast dissolving oral thin film containing dexamethasone: A possible application to antiemesis during cancer chemotherapy. PharmBiol. 2009;73(3):361-5. doi: 10.1016/j.ejpb.2009.08.010.
12. Borsadia SB, O'Halloran D, Osborne JL. Quick-dissolving films: A novel approach to drug delivery. Drug Deliv Technol.2003;3:1.
13. Ahmed M, Charyulu R, Harish N, Prabhu P. Formulation and *in-vitro*evaluation of chitosan films containing tetracycline for the treatment of periodontics. Asian J Pharm. 2009;3(2):113-9. doi: 10.4103/0973-8398.55048.
14. Niamsa N, Baimark Y. preparation and characterization of highly flexible chitosan films for use as food packaging. Am J Food Technol. 2009;4(4):162-9. doi: 10.3923/ajft.2009.162.169.