JOURNAL OF PHARMACEUTICAL SCIENCE AND BIOSCIENTIFIC RESEARCH (JPSBR)

(An International Peer Reviewed Pharmaceutical Journal that Encourages Innovation and Creativities)

Development of Stable Formulation and Evaluation of Combination of Amoxycillin and Clavulanic Acid

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ABSTRACT:

The present work is aimed to develop a stable formulation of preferred combination of two antibiotics -Amoxycillin and Clavulanic acid to overcome packaging instability resulting in to swelling of blister pack due to their interaction causing gas generation. Amoxycillin and Clavulanic acid dispersible tablets were prepared by dry granulation method using different superdisintegrants i.e. Croscarmellose, Crospovidone and Sodium Starch Glycolate. 15°C temperature and 20%RH humidity were throughout maintained. Aspartame as a sweetener and pineapple flavor were used to increase palatability. The prepared tablets were evaluated for hardness, friability, Disintegration time and Wetting time and in vitro drug release. Analytical estimation was done by HPLC. Amoxycillin and Clavulanic acid dispersible tablets were found to be of good quality fulfilling all the requirements for tablets. The results indicated that concentration of Crospovidon, Croscarmellose sodium, Sodium starch glycolate significantly affected. Croscarmellose Sodium showed least friability, disintegration time as compared to batches prepared from Sodium starch glycolate and Crospovidon. Amoxycillin and Clavulanic acid dispersible tablets were successfully formulated by dry granulation technique with improved patient compliance & immediate onset of action.

Key Words: Dispersible tablets, Amoxycillin and Clavulanic acid, Stability, dry granulation, Croscarmellose sodium, Disintegration time.

Article history:
Received 19 Aug 2013
Accepted 01 September 2013
Available online 13 September2013

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INTRODUCTION:

The oral route of drug administration is the most popular and successfully used for conventional delivery of drugs[1]. It offers the advantages of convenience, ease of administration, greater flexibility in dosage form design, ease of production, and low cost. It is probable that almost 90% of all the drugs are administered by oral route. [2]

"Dispersible tablets are uncoated or film-coated tablets that produce a uniform dispersion in water and may contain permitted flavoring and sweetening agents." Dispersible tablets usually disintegrate within three minutes when put in water or a small amount of breast milk. [3]

Advantages of dispersible tablets are dispersible tablet is a convenient method of supplying pre measured amount of drug for relatively rapid dissolution, more convenient for active pharmaceutical ingredients with insufficient stability in water, provides several advantages over conventional solid dosage forms. The palatable dispersion formed after addition of dispersible tablet in water can be easily used by patients (i.e. pediatrics and geriatrics) who physically or

psychologically for relatively rapid dissolution, more convenient for active pharmaceutical ingredients with insufficient stability in water, provides several advantages over conventional solid dosage forms. The palatable dispersion formed after addition of dispersible tablet in water can be easily used by patients (i.e. pediatrics and geriatrics) who physically or psychologically unable to swell tablets and capsules. Dispersible tablets are intended to disperse in water before administration, so drugs remain in solid dosage form till it is consumed. Therefore Dispersible tablets have advantages of both solid and liquid dosage forms, i.e. portable dosage form, long shelf life, temper-proof dosage form, low cost and faster rate of production, easy and cheap to package and ship, rapid onset of action and hence quick onset of action, relatively large dose of dug can be administered by dispersible tablets as compare to orodispersible tablets and mouth dissolving film, easy to dispense and: they require minimal manipulation by health professionals and parents prior to use which minimizes the risk of errors. [4]

Amoxicillin Clavulanic acid dispersible tablet is used to treat certain infections caused by bacteria, including infections of the ears, lungs, sinus, skin, and urinary tract. Amoxicillin is in a class of medications called penicillin-like antibiotics. It works by stopping the growth of bacteria. Clavulanic acid is in a class of medications called beta-lactamase inhibitors. It works by preventing bacteria from destroying amoxicillin. [5, 6]

On the basis of market product evaluation, blister packings containing this formulation are noticed swollen i.e. mainly because degradation of Amoxycillin trihydrate in to solid plus gas by hydrolysis. [7] To meet this challenge there were two dimensions:

1. To develop stable formulation of Amoxicillin trihydrate and Clavulanate
   Potassium dispersible tablets, so as to avoid degradation of Amoxycillin Trihydrate
2. Blister pack may be replaced by strip pack.

To develop the formulation with good palatability and good mechanical strength as these are the crucial parameters to be considered while developing a dispersible tablet.[8]

The effect of selected process parameters on critical properties of dispersible tablets were studied, on the basis of disintegration time, wetting time, uniformity of dispersion, friability, hardness and dissolution profile.

MATERIALS AND METHODS

Amoxycillin Trihydrate IP, Clavulanate Potassium, Avicel pH 112, Crosscarmellose Sodium, Sodium Starch Glycolate, Polyplasdone XL, Magnesium Stearate IP, Talc IP, Aerosil USNF, Orange flavor, Pineapple flavor, Sunset yellow color, Quinoline yellow color, Aspartame BP were obtained as a gift sample from Cadila Pharmaceuticals Limited (Dholka, Ahmedabad).

Method: Dry granulation [9]

In the present research work, dispersible tablets of Amoxycillin and Clavulanic acid is formulated using dry granulation method. Wet granulation method was not used because this formulation is highly sensitive to moisture and temperature conditions. Preliminary trials were taken by using direct compression method and poor flow of the blend was observed. Therefore, dry granulation method is selected for all future batches.

As the Clavulanic acid is hygroscopic and thermo labile, the processing condition is continuously maintained at 15°C and 20% RH and at higher temperature condition Clavulanic acid showed discoloration due to degradation.

Procedure:

Table 1: Formulation of batches

FORMULATION INGREDIENTS	Quantity for 1 tablet (mg)
Amoxycillin trihydrate	400
Clavulanate potassium: MCC	142.56
Avicel pH 112 (MCC)	253.44
Croscarmellose sodium	19.22
Talc	4.5
Magnesium stearate	9
Croscarmellose sodium	19.22
Talc	9
Aspartame	14
Flavor orange DC 116	14
Sunset yellow color	4.28
Colloidal silicon dioxide	4.5
Magnesium stearate	9
Total Weight	**902.72**

Amoxycillin Trihydrate was sifted through #20 and Clavulanate Potassium, Avicel pH 112, Superdisintegrant, Colloidal silicon dioxide, Talc were sifted through #40. Both blends were mixed. Magnesium Stearate was sifted through #60 and mixed with the blend in polybag. Slugging of blend was done by using 20 mm round shape punch. 1.8 gm average weight and 6-10kg/cm2 hardness was set. Slugs were milled by using 1.0 mm screen in multimill. Milled blend sifted through #24. Remaining amount of Superdisintegrant. Aspartame, Flavor, and Talc were sifted through #40 and color sifted through #60.

OPTIMIZATION OF DIFFERENT FORMULATION PARAMETERS: [9, 10, 11]

1. **PROCESSING CONDITION**

Table 2: Different processing condition

Batch Code	T1	T2	T3
Operating Condition	15°C and 20% RH	25°C and 30%RH	35°C and 40% RH

2. SUPERDISINTEGRANTS [8]

Table 3: Different superdisintigrants

VARYING INGREDIENT	TYPE	Quantity for 1 tablet (mg) FORMULATION BATCH CODE					
		A1	**A2**	**A3**	**A4**	**A5**	A6
Sodium starch glycolate	(Intragranular)	7.69	11.53	15.38	19.22	23.07	**26.91**
	(Extragranular)	7.69	11.53	15.38	19.22	23.07	**26.91**
		B1	**B2**	**B3**	**B4**	**B5**	B6
Cross carmellose sodium	(Intragranular)	1.92	3.84	7.69	11.53	15.38	19.22
	(Extragranular)	1.92	3.84	7.69	11.53	15.38	19.22
		C1	**C2**		**C3**	C4	
Crospovidone/ Polyplasdone XL	(Intragranular)	7.69	11.53		15.38	**19.22**	
	(Extragranular)	**7.69**	**11.53**		**15.38**	**19.22**	

3. SWEETENER AND FLAVOR

Table 4: Different amount of sweetener and flavoring agent

VARYING INGREDIENT	Quantity for 1 tablet (mg) FORMULATION BATCH CODE		
	S1	**S2**	S3
Aspartame	10	14	**20**
Pineapple DC 106	**10**	**14**	**20**

4. COLOUR

Table 5: Formulation of batches by using Different amount of color

VARYING INGREDIENT	Quantity for 1 tablet (mg) FORMULATION BATCH CODE					
	F1	**F2**	**F3**	**F4**	**F5**	F6
Sunset yellow color	2.14	4.28	6.42	-	-	-
Quinoline yellow color	-	-	-	**2.14**	**4.28**	**6.42**

In polybag blends were mixed. Magnesium stearate was sifted through #60 and mixed with the blend in polybag properly. Blend was compressed to prepare tablets.

EVALUATION AND RESULTS

1. DRUG EXCIPIENT COMPATIBILITY

Drug excipients interaction was checked out by comparing the FTIR spectra of pure drug amoxycillin trihydrate, clavulanate potassium and FTIR spectra of the physical mixture of drug + excipients.
(Figure: 1)

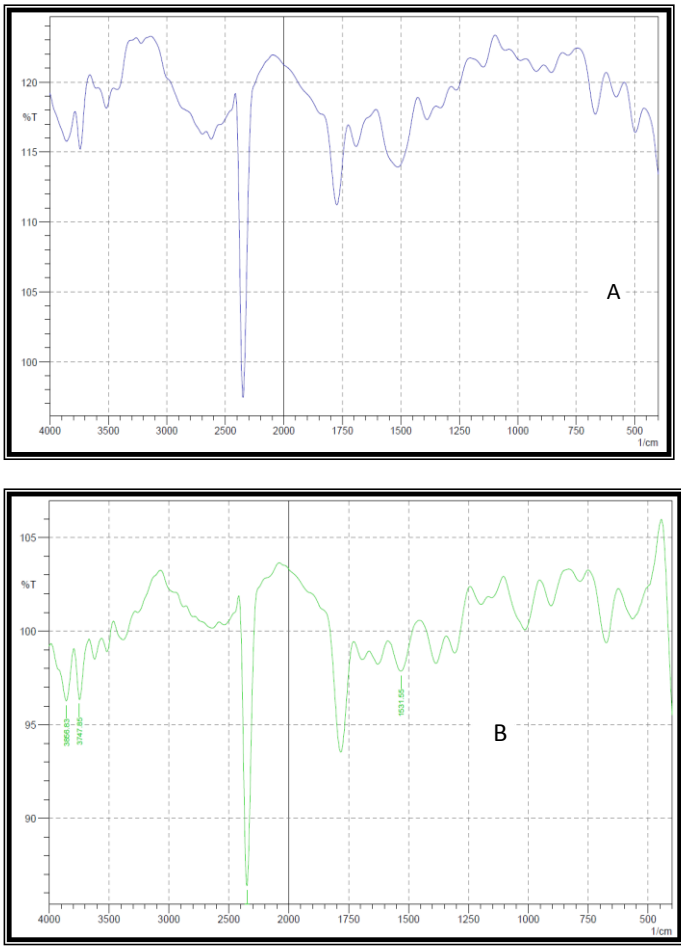

Figure 1 . FTIR spectra of (A)Amoxycillin trihydrate & (B) lavulanate potassium

IR spectra indicate no significant difference in characteristic peak at wave numbers of the drug in presence of the excipient. Thus, IR spectra indicated no drug-excipient interaction. (Figure 2)

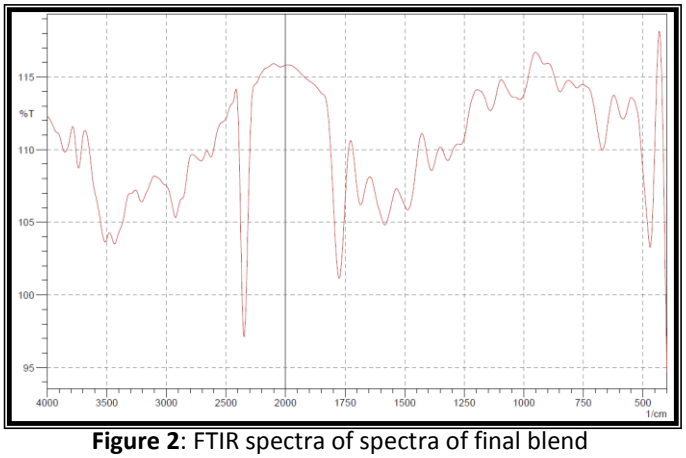

Figure 2: FTIR spectra of spectra of final blend

1. PRECOMPRESSION

Table 6: Precompression parameters

Batch	Angle of repose (θ)	Bulk density (gm/ml)	Tapped density (gm/ml)	%Carr's index	Hausner's ratio
A1	28.53	0.702	0.954	26.39	**1.358**
A2	25.11	0.802	0.954	26.38	**1.358**
A3	25.24	0.802	0.954	26.38	**1.358**
A4	25.81	0.684	0.955	26.18	**1.396**
A5	26.33	0.684	0.955	26.18	**1.396**
A6	27.89	0.434	0.555	21.74	**1.278**
B1	27.11	0.434	0.555	21.74	**1.278**
B2	24.88	0.429	0.562	23.42	**1.282**
B3	25.60	0.545	0.714	23.64	**1.309**
B4	24.51	0.545	0.714	23.64	**1.309**
B5	25.28	0.545	0.714	23.64	**1.309**
B6	**24.62**	**0.545**	**0.714**	**23.64**	**1.309**
C1	24.81	0.540	0.728	25.89	**1.349**
C2	25.33	0.600	0.705	15.00	**1.176**
C3	24.76	0.600	0.705	15.00	**1.176**
C4	**24.24**	**0.605**	**0.756**	**20.00**	**1.25**

2. IN VITRO DRUG RELEASE STUDY[13]

Determination of drug release from the disintegrated tablets was carried out in a USP-II paddle apparatus by using 900 ml of water at 37±0.5º as dissolution medium.The sample was taken after various time intervals and absorbance was measured using HPLC.

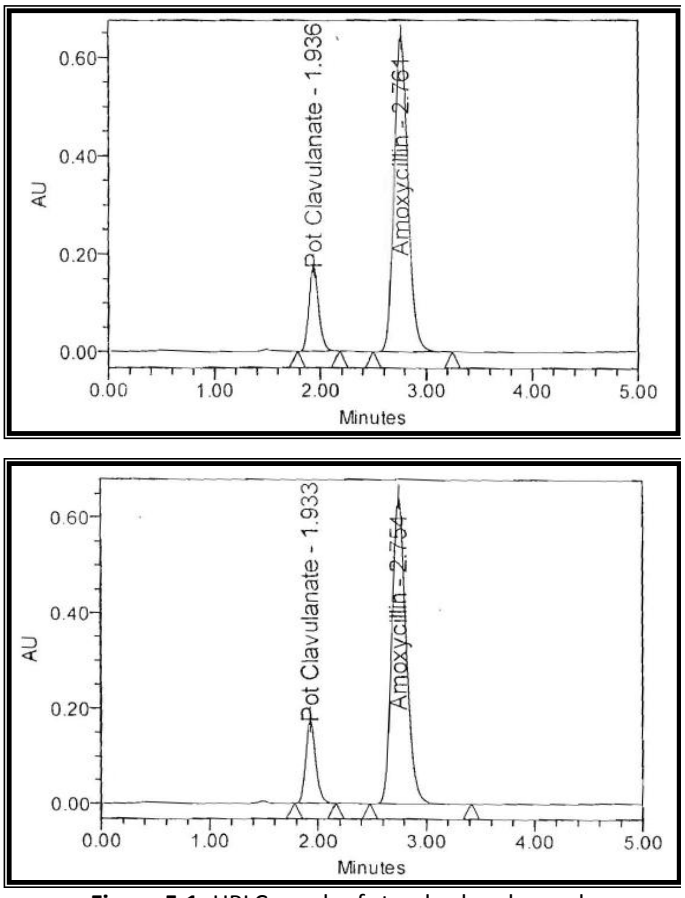

Figure 5.1: HPLC graph of standard and sample

3. FORMULATION PARAMETERS[12]

Table 7. Evaluation of formulated batches using Different Superdisintigrants

TEST PARAMETERS	RESULTS															
	A1	**A2**	**A3**	**A4**	**A5**	**A6**	**B1**	**B2**	**B3**	**B4**	**B5**	**B6**	**C1**	**C2**	**C3**	**C4**
Average wt (mg)	900	900	900	900	900	900	900	900	900	900	900	**900**	900	900	900	**900**
Thickness(mm)	6-6.2	6-6.2	6-6.2	6-6.2	6-6.2	6-6.2	6-6.2	6-6.2	6-6.2	6-6.2	6-6.2	**6-6.2**	6-6.2	6-6.2	6-6.2	**6-6.2**
Hardness(kg/cm^2)	7	9	5	10	12	13	4	5	7	9	10	**12**	5	7	9	**11**
Friability (%)	0.6	0.5	0.7	0.4	0.3	0.2	0.7	0.4	0.5	0.4	0.2	**0.2**	0.54	0.41	0.32	**0.21**
Wetting time (sec)	123	117	106	104	97	92	103	94	86	81	73	**69**	102	93	89	**81**
Uniformity of dispersion	FAIL	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS	**PASS**	FAIL	FAIL	PASS	**PASS**
Disintegration time (sec)	**82**	**76**	**58**	**59**	**72**	**95**	**78**	**69**	**61**	**54**	**45**	**42**	**85**	**71**	**67**	**58**

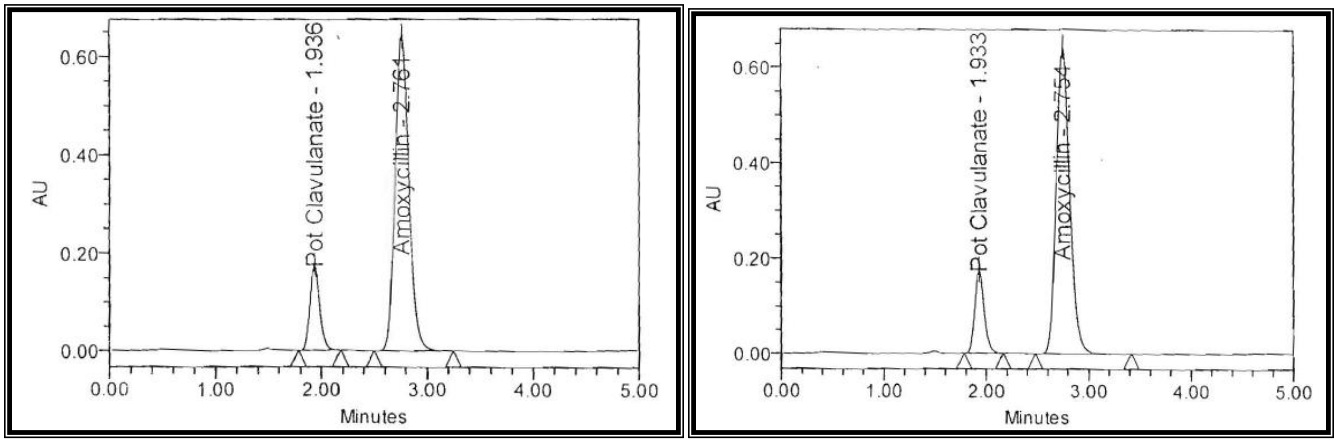

Figure 5.1: HPLC graph of standard and sample

Table 7. % Cumulative drug release of formulated batches using Different Superdisintigrants

TIME	CUMULATIVE % DRUG RELEASE (MEAN ± S.D.)															
	A1	A2	A3	A4	A5	A6	B1	B2	B3	B4	B5	B6	C1	C2	C3	C4
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5 SEC	43.55 ±0.17	49.22±0.25	65.51±0.29	49.78±0.15	55.45 ± 0.28	69.16 ±0.08	52.41 ±0.15	49.23 ±0.15	52.78 ±0.15	57.48 ±0.63	68.51 ±0.05	71.13 ±0.35	42.48 ±0.63	52.41 ±0.15	56.22 ±0.24	68.51 ±0.05
10 SEC	52.55 ±0.23	61.54±0.33	72.43±0.15	65.22±0.06	65.34 ±0.56	71.31 ±0.61	60.55 ±0.23	63.54 ±0.22	69.22 ±0.06	67.25 ±0.56	76.43 ±0.15	82.45 ±0.61	57.25 ±0.56	60.55 ±0.23	61.54 ±0.33	76.43 ±0.15
30 SEC	65.45 ±0.58	75.34±0.14	82.2 ±0.24	70.34±0.85	79.4 ±0.05	84.34 ±0.012	70.56 ±0.12	72.34 ±0.16	75.34 ±0.65	80.40 ±0.05	88.20 ±0.63	86.34 ±0.45	78.40 ±0.05	70.56 ±0.12	73.34 ±0.16	88.20 ±0.63
1 MIN	88.22 ±0.15	87.45±0.60	91.48±0.36	90.34±0.49	90.89 ±0.10	92.34 ±0.48	88.22 ±0.15	87.45 ±0.63	92.34 ±0.49	91.89 ±0.51	94.48 ±0.36	98.45 ±0.48	85.89 ±0.51	88.22 ±0.15	85.41 ±0.60	94.48 ±0.36
3 MIN	93.34 ±0.33	95.89±0.45	97.34±0.48	95.32±0.58	95.90 ±0.96	98.89 ±0.51	93.34 ±0.33	95.89 ±0.45	95.43 ±0.58	95.90 ±0.96	98.37 ±0.48	99.79 ±0.51	92.90 ±0.96	93.34 ±0.33	95.82 ±0.45	98.37 ±0.48
5 MIN	97.35 ±0.65	97.78±0.35	99.25±0.57	97.53 ±0.5	98.67 ±0.23	99.43 ±0.22	97.35 ±0.65	97.78 ±0.35	97.55 ±0.5	98.67 ±0.23	99.28 ±0.57	99.83 ±0.22	97.67 ±0.23	97.35 ±0.65	97.68 ±0.35	99.28 ±0.57
10 MIN	99.61 ±0.12	99.62±0.28	99.76±0.63	99.57±0.16	99.68 ±0.56	99.79 ±0.55	99.61 ±0.12	99.62 ±0.28	99.57 ±0.16	99.68 ±0.56	99.76 ±0.63	99.88 ±0.55	99.68 ±0.56	99.61 ±0.12	99.71 ±0.28	99.76 ±0.63
15 MIN	99.49 ±0.05	99.73±0.47	99.91±0.28	99.62±0.97	99.69 ±0.26	99.89 ±0.12	99.49 ±0.63	99.73 ±0.47	99.60 ±0.97	99.94 ±0.36	99.94 ±0.36	99.98 ±0.48	99.69 ±0.33	99.49 ±0.63	99.45 ±0.45	99.94 ±0.36

3. IN VITRO DRUG RELEASE STUDY[13]

Determination of drug release from the disintegrated tablets was carried out in a USP-II paddle apparatus by using 900 ml of water at 37±0.5º as dissolution medium.The sample was taken after various time intervals and absorbance was measured using HPLC.

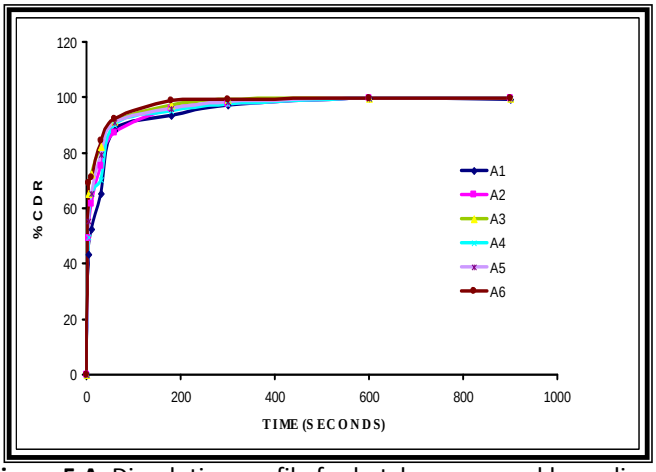

Figure 5 A. Dissolution profile for batches prepared by sodium starch glycolate

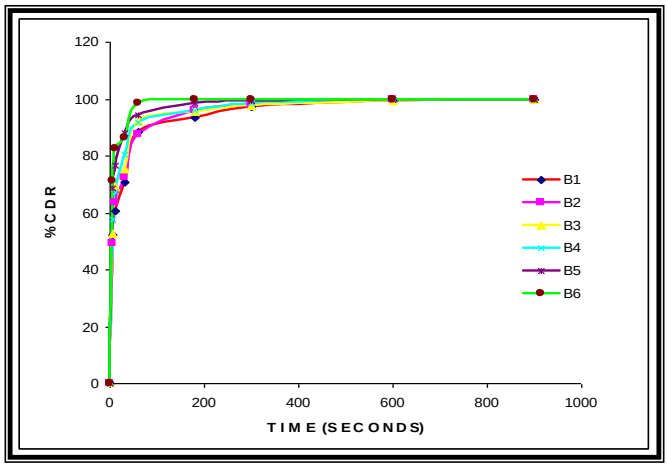

Figure 5 B. Dissolution profile for batches prepared by croscarmellose sodium

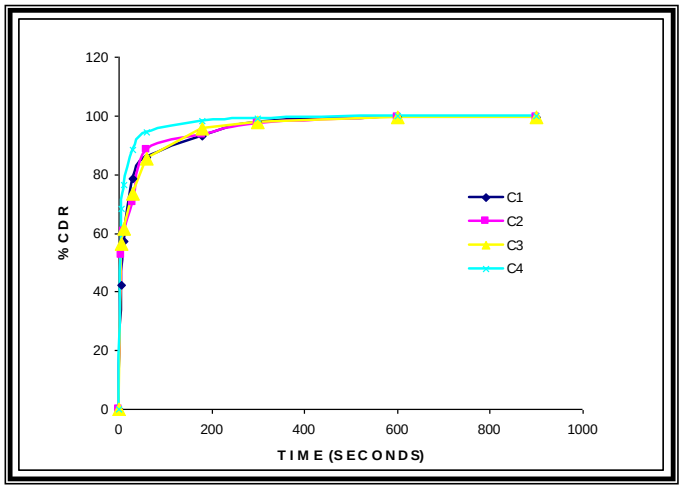

Figure 6: Dissolution profile for batches prepared by Crospovidon

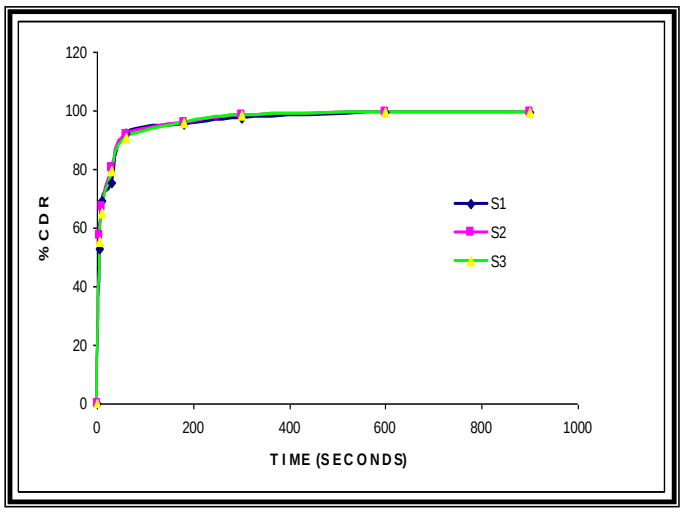

Figure 6 a. Dissolution profile for batches prepared by sweetener.

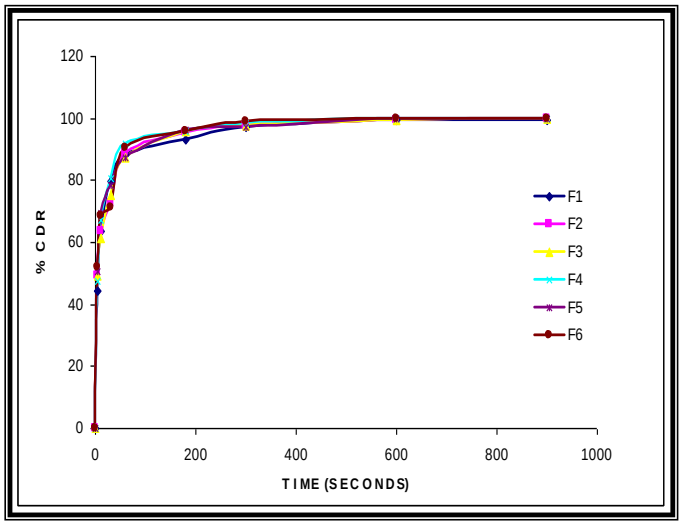

Figure 6 B. Dissolution profile for batches prepared by flavoring agent

DISCUSSION

1. PROCESSING CONDITION

Batch T2 showed slight discoloration of tablet because Clavulanate potassium is highly sensitive to temperature and humidity. Batch T3 showed sticking and picking problem during tablet compression and tablet discoloration was also observed. There was not any type of problem with Batch T1.So further trials were taken at 15°C and 20%RH.

2. SUPERDISINTEGRANTS

The batches A1 – A6 were prepared to explore the disintegration potential of Sodium starch glycolate. On addition of Sodium starch glycolate batch A1 and A2 showed increase in hardness and friability. Batch A3 and A4 showed disintegration time within one minute where as A1, A2, A5 and A6 showed disintegration time within 3 minutes. A3 showed minimum disintegration time but friability is more. All batches passed uniformity of dispersion except A1.

Table 7. %Cumulative drug release of formulated batches using Different sweetener and flavoring agent

TIME	CUMULATIVE % DRUG RELEASE (MEAN ± S.D.)								
	S1	S2	S3	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0	0	0	0
5 SEC	52.78 ±0.15	57.48 ±0.13	55.45 ±0.28	44.41 ±0.18	49.23 ±0.05	49.22 ±0.28	47.48 ±0.63	50.51 ±0.18	52.13 ±0.15
10 SEC	69.22 ±0.06	67.25 ±0.48	65.34 ±0.56	63.55 ± 0.36	63.54 ±0.42	61.54 ±0.23	67.25 ±0.56	69.43 ±0.15	68.45 ±0.61
30 SEC	75.34 ±0.65	80.40 ±0.05	79.4 ±0.05	79.56 ±0.21	72.34 ±0.16	75.34 ±0.15	80.40 ±0.05	78.20 ±0.26	71.34 ±0.74
1 MIN	92.34 ±0.49	91.89 ±0.51	90.89 ±0.10	88.22 ±0.15	88.45 ±0.13	87.45 ±0.63	91.89 ±0.51	87.48 ±0.36	90.45 ±0.48
3 MIN	95.43 ±0.58	95.90 ±0.96	95.9 ±0.96	93.34 ±0.33	95.15 ±0.45	95.89 ±0.45	95.90 ±0.96	96.37 ±0.48	95.92 ±0.53
5 MIN	97.55 ±0.5	98.67 ±0.03	98.67 ±0.23	97.35 ±0.05	97.78 ±0.35	97.78 ±0.35	98.67 ±0.23	97.28 ±0.57	98.96 ±0.22
10 MIN	99.57 ±0.16	99.68 ±0.56	99.68 ±0.56	99.49 ±0.12	99.62 ±0.24	99.62 ±0.28	99.68 ±0.51	99.76 ±0.63	99.79 ±0.53
15 MIN	99.60 ±0.97	99.69 ±0.33	99.69 ±0.26	99.61 ±0.03	99.73 ±0.57	99.81 ±0.47	99.92 ±0.36	99.94 ±0.69	99.89 ±0.49

The batches B1 – B6 were prepared to explore the disintegration potential of Croscarmellose Sodium. Addition of Croscarmellose Sodium in the batch B1 – B6 showed improvement in hardness and friability. Table showed that increase in the concentration of Croscarmellose Sodium, the disintegration time decreases and at the same time wetting time decreases. The batches prepared using Croscarmellose Sodium showed lower friability and disintegration time. The batches B3, B4 and B5 showed disintegration time less than one minute while batches B1, B2 and B3 showed disintegration time less than 3 minute. B6 batch showed best results amongst all batches on the basis of hardness, friability and disintegration time. Croscarmellose Sodium showed lower friability, disintegration time than Sodium starch glycolate batches. All of the prepared batches passed from uniformity of dispersion. Optimized concentration of croscarmellose sodium was found to be 5%.

The batches C1 – C4 were prepared to explore the disintegration potential of Polyplasdone XL. Addition of Polyplasdone XL in the batch C1 – C4 showed improvement in hardness and friability. Table showed that increase in the concentration of Polyplasdone XL, the disintegration time decreases and at the same time wetting time decreases. The batches prepared using Polyplasdone XL showed lower friability and disintegration time. The batch C4 showed disintegration time less than one minute while batches C1, C2 and C3 showed disintegration time less than 3 minute. Batches prepared using Polyplasdone XL showed more disintegration time as compare to batches prepared from croscarmellose sodium.

Formulation batches prepared by using Croscarmellose sodium showed minimum disintegration time, wetting time, friability, sufficient hardness and good uniformity of dispersion as compare to batches that were prepared by using Sodium starch glycolate and Crospovidon. Optimized concentration of Croscarmellose sodium was found to be 5%.

3. SWEETENER AND FLAVOR

Batches S1 to S3 prepared by using 0.12%, 0.16%, 0.24% of Aspartame and Flavor respectively. Batch S1 didn't show appropriate sweetness and flavor. Batch S2 showed acceptable sweetness, flavor and appropriate palatability. Where as, batch S3 showed more amount of sweetness and flavor that is not needed. So final optimized concentration of sweetener and flavor was found to be 0.16% and pineapple flavor showed excellent result by tasting as compare to orange flavor. So in the final formulation pineapple flavor will be preferred.

4. COLOUR

Batches F1 to F6 prepared by using 0.25%, 0.5%, and 0.75% of colors. Batches F4, F5 and F6 showed more elegant color and uniformity of color distribution as compare to F1, F2 and F3 batches. Batch F5 showed most elegant appearance. So optimized color quinoline yellow at concentration 0.50% was found to be most appropriate.

STABILITY TESTING FOR FINAL PRODUCT

A) Packing: Alu- Alu Blister:

Table 14. Stability testing at different temperature in blister packing

Physical parameters	**2 to 8°C**			**25± 2°C ,60 ± 5% RH**			**40± 2°C ,75 ± 5% RH**		
	Initial	**1 M**	**2M**	**Initial**	**1 M**	**2M**	**Initial**	**1 M**	**2M**
Appearance	Good	Good	Good	Good	Good	Good	Good	DC	DC
Weight gain (mg)	-	-	-	-	20	25	-	40	50
Percentage drug content (Amoxycillin trihydrate)	99.98	99.87	98.72	99.98	99.74	98.69	99.98	99.79	98.53
Percentage drug content (Clavulanate potassium)	99.84	99.75	98.53	99.84	99.64	98.51	99.84	99.68	98.44
Hardness (kg/cm2)	10	10	11	10	11	12	10	11	13
Disintegration time(sec)	44	47	53	44	48	55	44	52	55
Wetting time(sec)	71	75	79	71	78	80	71	78	90

DC= Discoloration, %Drug release

Table 15 %Drug release after stability period

Amoxycillin trihydrate			Clavulanate potassium		
SR NO	**TIME(month)**	**40± 2°C ,75 ± 5% RH**	**SR NO**	**TIME(month)**	**40± 2°C ,75 ± 5% RH**
1	0	99.99	1	0	99.99
2	1	98.84	2	1	98.78
3	2	98.56	3	2	98.62

Observation: Blister pack observed swollen after 2 months.

B) Packing: Strip pack.

Table 16 Stability testing at different temperature in strip packing

Physical parameters	2 to 8°C			25± 2°C ,60 ± 5% RH			40± 2°C ,75 ± 5% RH		
	Initial	**1 M**	**2M**	**Initial**	**1 M**	**2M**	**Initial**	**1 M**	**2M**
Appearance	Good	Good	Good	Good	Good	Good	Good	DC	DC
Weight gain (mg)	-	-	-	-	20	25	-	40	50
Percentage drug content (Amoxycillin trihydrate)	99.98	99.91	98.85	99.98	99.83	98.79	99.98	99.76	98.1
Percentage drug content (Clavulanate potassium)	99.92	99.89	98.83	99.92	99.87	98.81	99.92	99.67	98.4
Hardness (kg/cm2)	10	10	11	10	11	12	10	11	13
Disintegration time(sec)	44	45	48	44	51	57	44	53	59
Wetting time(sec)	71	72	76	71	76	79	71	74	82

Table 17. %Drug release after stability period

Amoxycillin trihydrate			Clavulanate potassium		
SR NO	**TIME(month)**	**40± 2°C ,75 ± 5% RH**	**SR NO**	**TIME(month)**	**40± 2°C ,75**
1	0	99.99	1	0	99.99
2	1	99.95	2	1	99.78
3	2	99.61	3	2	99.67

OBSERVATION:

Strip pack showed excellent product stability. Results of 2 months accelerated stability data (40°C ± 2°C/75% RH ± 5% RH) found satisfactory. There is no significant change in results from initial.

CONCLUSION

15°C temperature and 20%RH was optimized for tablet manufacturing process. Croscarmellose Sodium showed least friability and disintegration time as compared to batches prepared from Sodium starch glycolate and Crospovidone. 5% concentration of Croscarmellose sodium was optimized as it served all the desirable criteria. Optimized concentration of Aspartame as a sweetener and pineapple flavor was found to be 0.16%. Optimized concentration of color was found to be 0.5%. Optimized batch B6 containing 5% of Croscarmellose sodium showed disintegration time 45-50 seconds, wetting time 67-70 seconds, hardness 10-12 kg/cm^2, excellent palatability, 98.45% drug release within 1 minute and produced uniform dispersion in water, hence could meet the desired specifications. Optimized formulation showed superior product stability and dissolution profile with less disintegration time. Short-term stability studies on the formulation indicated that there are no significant changes in drug content and in vitro disintegration time.

The present study underlines the importance of formulation and processing variables. By using optimum amount of Superdisintegrants, it is possible to prepare Amoxycillin and Clavulanic acid dispersible tablets with acceptable mechanical strength and rapid disintegration, to provide desired drug release property and pleasant mouth feel which may overcome stability problem by replacing blister pack by strip pack.

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