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Research Article

Effect of Diluents on Immediate Release Tablet of Hydrochlorothiazide

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ABSTRACT

The current study is aimed to study the effect of diluents on the immediate release tablet of hydrochlorothiazide. The diluents used are Avicel PH 101 and starlac. Various flow properties are determined for the powder blend and optimised within the range with the help lubricants and glidants. Final bulk is maintained with the help of diluents mainly Avicel PH 101 and starlac. Final tablet are evaluated for various parameters like thickness and diameter, hardness, disintegration time, friability and dissolution rate etc. As the formulation contains diluents in major quantity the effect of these diluents drug release rate is examined. With increase in amount of disintegrating agent release rate is increased up to certain level and then decrease. Release rate of formulations containing Avicel PH 101 is faster as compared to starlac.

INTRODUCTION

Tablet dosage form had been remained as attractive since many years. Though there are many variations like conventional tablet, sustained release tablet, and immediate release tablet. Out of which immediate release dosage forms are developed to release the drug at faster rate as compared to conventional dosage forms. It can be achieved with the help of disintegrating agents. Selection of diluents is also important factor to have optimum drug release. In the present formulation hydrochlorothiazide is used as model drug as it is well absorbed through gastrointestinal tract [1]. Hydrochlorothiazide belongs to the thiazide class of diuretics, acting on the kidneys to reduce sodium reabsorption in the distal convoluted tubule. This increases the osmolarity in the lumen, causing less water to be reabsorbed by the collecting ducts. This leads to increased urinary output [2]. Avicel PH 101 and starlac are used as diluents and Ac-di-sol is used as disintegrating agent. Avicel PH 101 is microcrystalline cellulose. Ac-di-sol is cross linked carboxymethylcellulose sodium and composition of starlac is of 15% starch and 85% lactose.

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MATERIALS AND METHODS

Hydrochlorothiazide was supplied by Wallace Pharmaceuticals Pvt. Ltd, Goa, Ac-di-sol, starlac and Avicel PH 101 was obtained from the signet chemical corporation, Mumbai. All the ingredients were of pharmaceutical grade. Other materials and solvents used were of analytical grade.

EXPERIMENTAL

Preparation of tablet

The tablets are prepared by direct compression method. All the ingredients and drug were properly sieved through 40 meshes. The filler was blended properly with hydrochlorothiazide the above blend was lubricated with aerosil, and magnesium stearate. Powder blend were evaluated for various flow properties. Finally tablets were prepared by direct compression.
All the formulations are shown in Table 1.

Evaluation of Powder Blend

1. Angle of Repose [3]

Angle of repose has been defined as the maximum angle possible between the surface of pile of powder and horizontal plane. The angle of repose was determined by the funnel method.The angle of repose was calculated by substituting the values of the base radius 'r' and pile height 'h' in the following equation:

$$\theta = \tan^{-1}(h/r)$$

θ = Angle of repose, h = height of the pile
r = radius of the pile

Bulk Density [3]

The bulk density was obtained by dividing the mass of a powder by the bulk volume in cm^3. The sample of about 50 cm^3 of powder, previously been passed through a standard sieve no. 20, was carefully introduced into a 100 ml graduated cylinder. The bulk density of each formulation was then obtained by dividing the weight of sample in grams by the final volume in cm^3 of the sample contained in the cylinder.

$$\text{Bulk density} = \frac{\text{Weight of powder}}{\text{Bulk volume}}$$

Tapped Density [3]

The tapped density was obtained by dividing the mass of a powder by the tapped volume in cm^3. The sample of about 50 cm^3 of powder, previously been passed through a standard sieve no. 20, is carefully introduced into a 100 ml graduated cylinder. Tap density was measured using digital tap density test apparatus. The tapped density of each formulation was then obtained by dividing the weight of sample in grams by the final tapped volume in cm^3 of the sample contained in the cylinder.

$$\text{Tapped density} = \frac{\text{Weight of powder}}{\text{Tapped volume}}$$

Hausner ratio [3]

Hausner's ratio indicates the flow properties of powder and measured by the ratio of tapped density to bulk density. Hausner's ratio was determined by the given formula

$$\text{Hausner's ratio} = \frac{TD}{BD}$$

Carr's compressibility Index[3]:

The percentage compressibility of a powder was a direct measure of the potential powder arch or bridge strength and stability. Carr's index of each formulation was calculated according to equation given below:

$$\text{Carr's Index} = \frac{(TD-BD)}{TD} \times 100$$

Evaluation of tablets

A. Thickness and Diameter [4]

Thickness and diameter of tablets were determined using Vernier calliper scale. Five tablets from each batch were used, and average values were calculated.

B. Uniformity of weight [4]

Twenty tablets were randomly selected from each batch individually weighed, the average weight and standard deviation of 20 tablets was calculated. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in and none deviates by more than twice that percentage. Percentage weight variation is calculated by the formula as below:

$$\text{Percentage weight variation} = \frac{(W_{avg} - W_{initial})}{(W_{avg})} \text{ X } 100$$

Where, W_{avg} = Average weight of tablet,
$W_{initial}$ = Individual weight of tablet.

C. Dissolution Studies [4]

The release rate of hydrochlorothiazide from fast dissolving tablets was determined using USP Dissolution Testing Apparatus II (Paddle type). The dissolution test was performed using 900 ml of 0.1 N HCl, at 37 ± 0.5^{0}C and 100 rpm. A sample (10 ml) of the solution was withdrawn from the dissolution apparatus every 1 min. and the samples were replaced with same volume of fresh dissolution medium. The test was carried out for 20 min. The samples were filtered through whatman filter paper no. 41. Absorbance of these solutions was measured at 272.5 nm using UV spectrophotometer Shimadzu 1700. Cumulative percentage drug release was calculated using an equation obtained from a standard curve.

D. Disintegration Test [4]

Disintegration is carried out to ensure that the drug substance is fully available for dissolution and absorption from the gastrointestinal tract. This test was carried out using tablet disintegration test apparatus. The medium used for disintegration test was 0.1 N HCl temperature of 37±2^{o}C.

E. Friability [5]

Twenty tablets were weighed and placed in the Roche friability test apparatus. Apparatus was rotated at 25 rpm for 4 min. after revolution the tablets were dusted and reweighed

$$\% \text{ Friability} = \frac{(\text{Initial weight-Final weight})}{(\text{Initial weight})} \text{ X } 100$$

Table 1: Formulation of immediate release tablets of hydrochlorothiazide

Ingredients	A1	A2	A3	A4	S1	S2	S3	S4
Hydrochlorothiazide	25	25	25	25	25	25	25	25
Avicel PH 101	72.5	71.5	70.5	69.5	-	-	-	-
Starlac	-	-	-	-	72.5	71.5	70.5	69.5
Ac-di-Sol	1	2	3	4	1	2	3	4
Magnesium stearate	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Aerosil	1	1	1	1	1	1	1	1
Sunset Yellow	q.s.	q.s.	q.s.	q.s.	-	-	-	-
Quinoline Yellow	-	-	-	-	q.s.	q.s.	q.s.	q.s.
Total weight	100	100	100	100	100	100	100	100

Table 2: Evaluation of powder flow properties

Formulation	Angle of repose	Bulk density (gm/cm^3)	Tap density (gm/cm^3)	Carr's compressibility index	Hausner's ratio
A1	20.64 ± 0.04	0.325 ± 0.03	0.227 ± 0.02	18.40%	0.698± 0.046
A2	26.41 ± 0.12	0.421 ± 0.02	0.20 ± 0.02	17.25%	0.475± 0.05
A3	25.24 ± 0.05	0.351 ± 0.04	0.227 ± 0.03	16.50%	0.646± 0.072
A4	27.03 ± 0.01	0.336 ± 0.03	0.294 ±0.02	20.04%	0.875±0.021
S1	21.33 ± 0.03	0.431 ± 0.01	0.357 ± 0.04	18.20%	0.828± 0.030
S2	27.6 ± 0.06	0.394 ± 0.02	0.279 ± 0.02	16.97%	0.708± 0.012
S3	24.14 ± 0.04	0.407 ± 0.03	0.246 ± 0.03	19.52%	0.604± 0.042
S4	26.33 ± 0.03	0.354 ± 0.04	0.274 ± 0.01	17.24%	0.774± 0.001

* Each sample was analysed in triplicate (n = 3)

Table 3: Evaluation of immediate release tablets of hydrochlorothiazide

Formulation	PARAMETER'S					
	Thickness (mm)	Diameter (mm)	Disintegration time (seconds)	Friability	Hardness (kg/cm^2)	Drug Content
A1	1.56 ± 0.12	7.94± 0.02	072 ± 7	0.2 ± 0 .23	4.5 ± 0.30	98.56 ± 0.25
A2	1.50 ± 0.17	7.95 ± 0.02	065 ± 6	0.4 ± 0.12	3.9 ±0.24	100.21 ± 0.84
A3	1.54 ± 0.23	7.95 ± 0.01	051 ± 6	0.2 ± 0.24	4.7 ± 0.29	99.45 ± 0.67
A4	1.52 ± 0.31	7.96 ± 0.02	048 ± 5	0.3 ± 0.30	4.9 ± 0.31	99.64 ± 0.35
S1	1.50 ± 0.24	7.95 ± 0.01	114 ± 8	0.3 ± 0.16	4.2 ± 0.22	98.97 ± 0.28
S2	1.53 ± 0.22	7.98 ± 0.02	103 ± 6	0.3 ± 0.20	4.7 ± 0.13	100.06 ± 0.47
S3	1.52 ± 0.27	7.96 ± 0.03	084 ± 5	0.4 ± 0.22	4.6 ± 0.28	99.87 ± 0.31
S4	1.55 ± 0.20	7.97 ± 0.03	068 ± 4	0.6 ± 0.31	4.8 ± 0.24	100.57 ± 0.52

* Each sample was analysed in triplicate (n = 3)

F. Hardness [5]

For each formulation, the hardness of five tablets was determined using the pfizer hardness tester. Tablet was fixed in the jaw of tester and dial reading is adjusted to the zero. Pressure is applied till tablet breaks or fractured and dial reading is noted.

Drug Content [6]

Twenty tablets were weighed and average weight was calculated. The tablets were crushed into fine powder. Tablet powder equivalent to 25mg of Hydrochlorothiazide was transferred separately to 100ml volumetric flask and sonicated for 10min .The volume was made upto the mark with distilled water and 0.01N NaOH. The resulting solution was then filtered through

a whatmann filter paper no. 41.Aliquot portion was appropriately diluted with distilled water and 0.01N NaOH to get final concentration of 20µg/ml of Hydrochlorothiazide. The concentrations of Hydrochlorothiazide were determined by measuring absorbance of sample at 272.5 nm in spectrum mode.

RESULT AND DISCUSSION

Evaluation of Powder Flow Properties

Angle of repose for the formulation A1 to A4 is varied from 20.64 to 27.03 and formulation containing starlac varied from 21.33 to 27.6. Bulk density was found in the range of 0.325 to 0.421 and 0.354 to 0.431 for Avicel PH 101 and starlac respectively. Tap density for A1 to A4 was varied from 0.20 to 0.294 and for starlac 0.246 to 0.357. Carr's compressibility index was found to be 16.50% to 20.04% for the formulation containing Avicel PH 101 and for starlac it was 16.97% to 19.52 %. All the formulation exhibit good flow properties and complies as per the I. P. Specifications. Results of the test are shown in the Table 2.

Evaluation of Tablet:

1. Tablet Thickness and Diameter: - Thickness and Diameter of the formulations A1 to A4 varied from 1.50 ± 0.17 to 1.56 ± 0.12 mm and 7.94 ± 0.02 to 7.96 ± 0.02 mm, while of formulations S1 to S4 showed from 1.50 ± 0.31 to 1.55 ± 0.20 mm and 7.95 ± 0.01 to7.98 ± 0.02 mm respectively.
2. Uniformity of Weight: Tablets from each batch showed uniformity of weight as per I.P. limits. Each sample was analyzed in triplicate (n = 3).
3. Disintegration test: Tablets from each batch show immediate disintegration. Disintegration time decreases with increase in concentration of the ac- di-sol.
4. Friability: Friability ranges from 0.2 to 0.3 for A1 to A4 and 0.3 to 0.6 for S1 to S4. Evaluated friability value indicates good mechanical strength.
5. Hardness: Hardness value ranges from 3.9 to 4.9 for A1 to A4 and 4.2 to 4.8 for S1 to S4.

In Vitro Dissolution Study

Formulation containing Avicel PH 101 as diluents, as the concentration of ac-di-sol was increased the disintegration time decreases and dissolution of drug increases. 100% drug was released from the all the formulation A1, A2, A3, A4 in 17, 14, 10, 10 minutes respectively. Dissolution profiles of the formulations A1, A2, A3, and A4 are shown in Fig. 1. For formulation having starlac as the diluent 100% drug were released from the all the formulation S1, S2, S3, S4 in 20, 17, 13, 10 minutes respectively. Dissolution profiles of the formulations containing starlac are shown in Fig. 2.

From drug release it was observed that increase in concentration of ac- di-sol increases the drug release up to 3% concentration in the tablet, but further increase in the concentration of ac- di-sol does not show any significant increase in the dissolution rate. Dissolution pattern of both the formulations are shown in Fig. 1 and 2

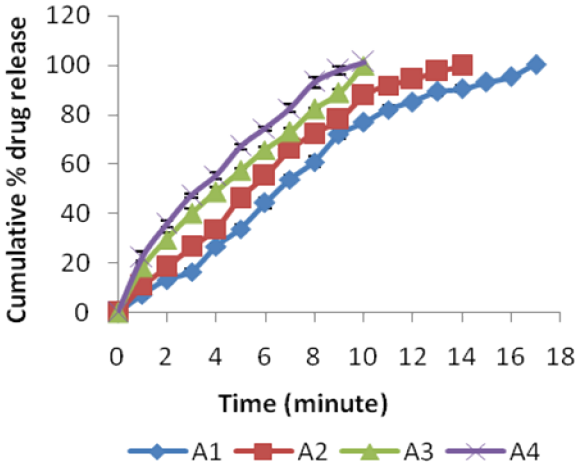

Figure 1: cumulative % drug release of the formulation containing Avicel pH101as a diluent.

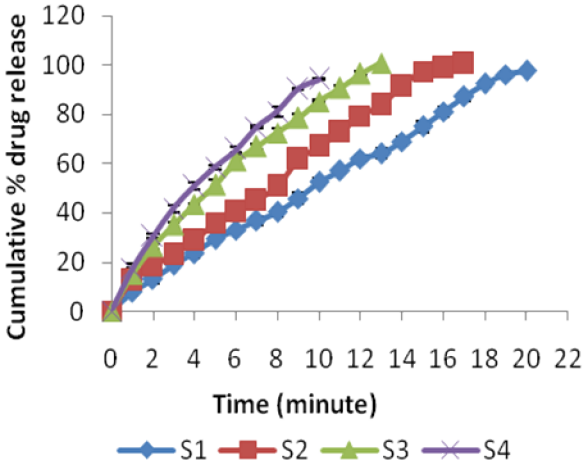

Figure 2: Cumulative % drug release of the formulation containing starlac as a diluent.

Effect of Diluents on Hydrochlorothiazide release

Effect of diluent on the release profile of Hydrochlorothiazide was observed. Formulation containing Avicel PH 101 gives faster release than that of starlac as diluent.

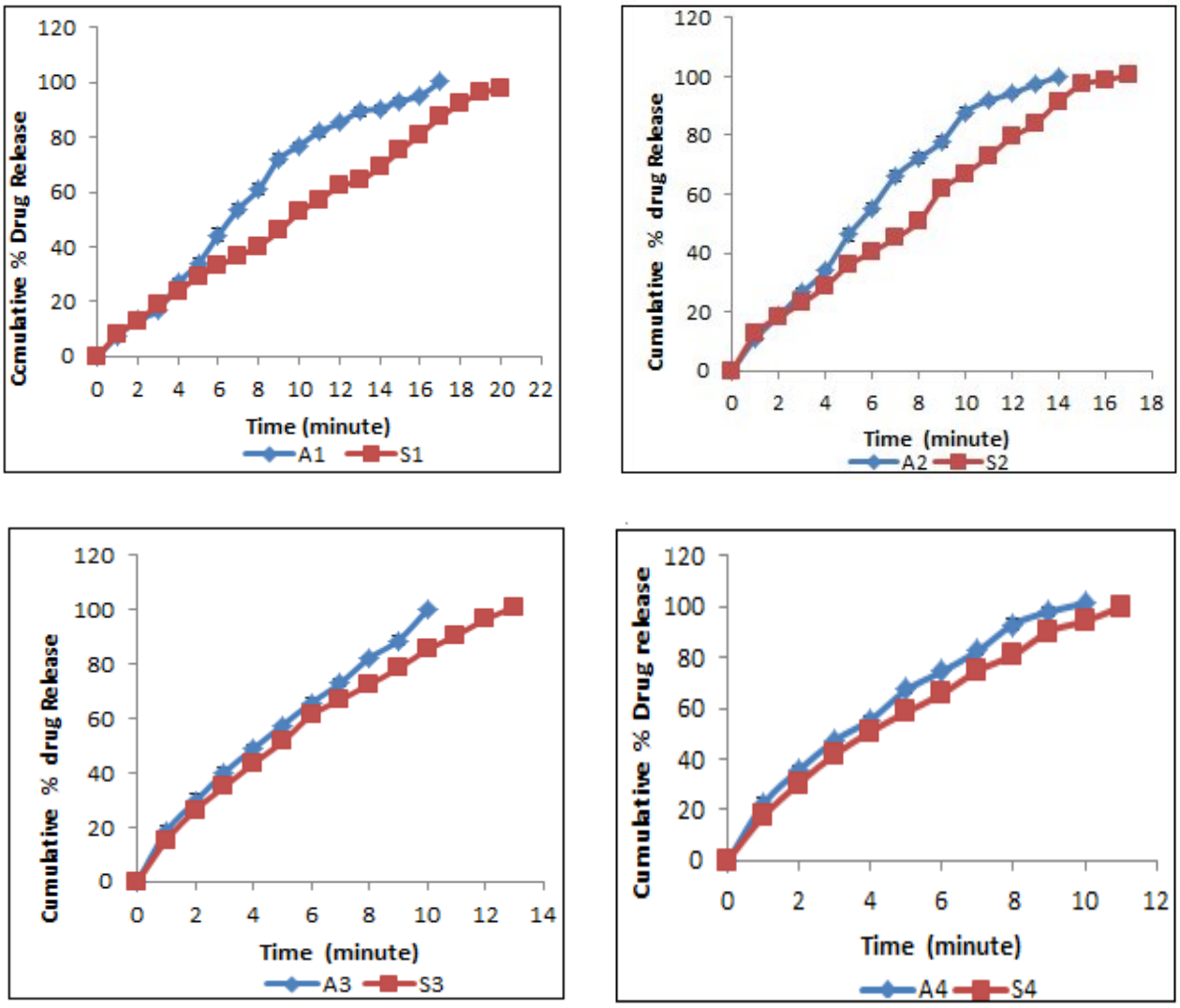

Figure 3: Effect of diluents on dissolution profile of drug.

It was observed that as the concentration of ac-di-sol increases, the water absorption ratio increases and disintegration time decreases,in the formulation containing Avicel PH 101.This effect may be the due to the capillary action or swelling of the Avicel PH 101 and formulations containing starlac as diluent, it was observed that ac-di-sol does not seem to have much significant effect on the water absorption ratio and disintegration time of the tablets [7]. So formulation A1, A2, A3, and A4, 100% of drug was released in 17, 14, 10, and 10 minutes respectively. While the S1, S2, S3, and S4 show 100% drug were released in 20,17,13,10 minutes respectively.

CONCLUSION

From the above results it can be concluded that Avicel PH101 and starlac both are effective for immediate release of the drug but Avicel PH101 can release the drug faster as compared to the starlac.

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