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Formulation, Optimization and Evaluation of Mouth Dissolving Tablet of Zidovudine

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ABSTRACT: ***The aim of the present study was to formulate and evaluate the mouth dissolving tablets of Zidovudine. Drug delivery systems are becoming more complex as pharmaceutical scientist acquires better understanding of the physiochemical & biochemical parameters pertinent to their performance, over the last decade. The demand of mouth dissolving tablet has been growing mainly for geriatric and pediatric patients, because of swallowing problem, the characteristics of mouth dissolving tablet for potential emergency treatment. The super disintegrants used in this study was sodium starch glycolate and croscarmellose sodium. The tablets were evaluated for weight variation, hardness, wetting time, friability, water absorption ratio and disintegration time and dissolution study. The tablets were prepared by direct compression method.***

KEYWORDS: ***Zidovudine, Mouth Dissolving Tablet, Sodium Starch Glycolate, Croscarmellose sodium, direct compression***

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INTRODUCTION:

Over the past one decade, there has been an enhanced demand for more patient friendly and compliant dosage forms. As a result, the demand for developing new technologies has been increasing, since the development cost of a new drug dosage forms for existing drugs with improved safety and efficacy, bioavailability together with reduced dosing frequency, and the production of more cost effective dosage forms.

Zidovudine an antiretroviral drug is widely used in the treatment of HIV infection. Zidovudine has good bioavailability (60-70 %). As the half-life of Zidovudine is very less (1 hr) so, pediatric patients have to administer the tablets of Zidovudine 3-4 times and women patients for the prevention of maternal to foetus transmission of HIV infection have to administer it about 4-5 times in a day. Also, the drug is very bitter in taste. Hence, the multiple dosing with bitter tasting drug reduces the patient compliance especially in case of pediatrics.

To overcome these problems mouth dissolving tablets are good option. Since, they disintegrate and dissolve rapidly in saliva without need for drinking water. The development of a fast dissolving tablet also provides an opportunity for a line extension in the market. Thus the present drug is chosen as a suitable candidate for the formulation of fast disintegrating tablet using two Superdisintegrants.

MATERIALS AND METHODS:

MATERIALS:

Zidovudine was obtained from Mylan Pharmaceuticals, Nashik. Sodium starch glycolate, crosscarmellose sodium was obtained from commercial sources. All other reagents were of analytical grade.

METHOD:

Mouth dissolving tablet were prepared using superdisintegrant addition. Different quantity of sodium starch glycol ate and crosscarmellose sodium was used. The quantity giving the

best disintegration time along with optimum hardness was chosen and tablets prepared by direct compression. The final formulae for preparation of MDT are given in table 1. Accurately weighed Zidovudine was mixed with sodium starch glycolate, cross carmellose sodium, mannitol, aspartame, microcrystalline cellulose for about 10 to 15 minutes. Then passed above mixture from sieve no. 60 to achieve uniform size particles and free flowing property. Then magnesium stearate was added and mixed for two minutes and compressed into tablet using double concave punches. The prepared tablets was evaluated for weight variation, friability, hardness, disintegration time, in vitro dissolution study as procedure given in Indian Pharmacopoeia.

Table 1: Formulation composition of Mouth Dissolving Tablets of Zidovudine

Ingredients (mg)	Formulation code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Zidovudine	300	300	300	300	300	300	300	300	300
Sodium starch glycolate	1.5	3	5	1.5	3	5	-	-	-
Croscarmellose sodium	-	-	-	1.5	3	5	1.5	3	5
Magnesium stearate	1	1	1	1	1	1	1	1	1
Aspartame	1	1	1	1	1	1	1	1	1
Microcrystalline Cellulose	50	50	50	50	50	50	50	50	50
Mannitol	146.5	145	143	145	142	138	146.5	145	143
Total	500	500	500	500	500	500	500	500	500

Preparation of calibration curve:

Weigh quantity of Zidovudine (100 mg) place in 100 ml of standard volumetric flask and make up the volume with simulated saliva pH 6.8. The stock solution obtained is 1000µg/ml solution. Aliquots of 0.5, 1.0, 1.5, 2.0 and 2.5 ml of stock solution pipette out into 100 ml standard volumetric flasks and final volume adjust up to 100 ml with simulated saliva pH 6.8 to give the concentration of 5, 10, 15, 20 and 25µg/ml. The absorbance measures at 266 nm in UV spectrophotometer against reagent blank with simulated saliva pH 6.8 (Table 2 and Figure 1)

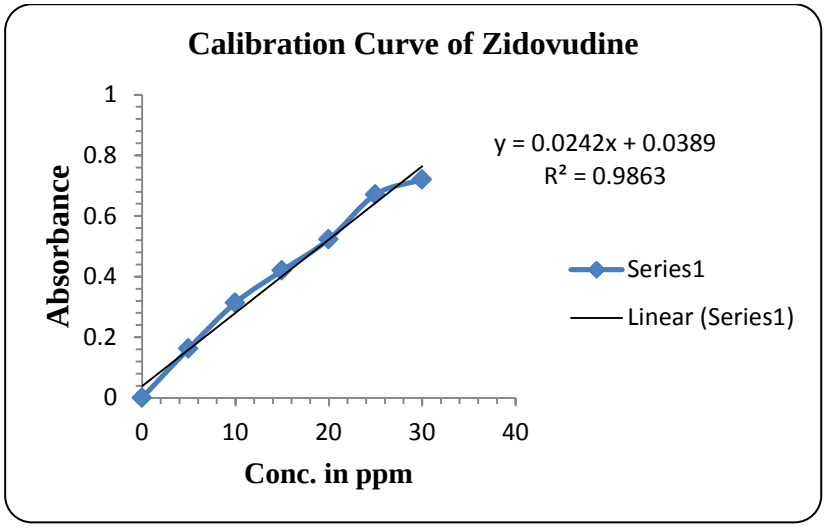


Figure 1: Calibration Curve of Zidovudine in Saline Phosphate buffer pH 6.8

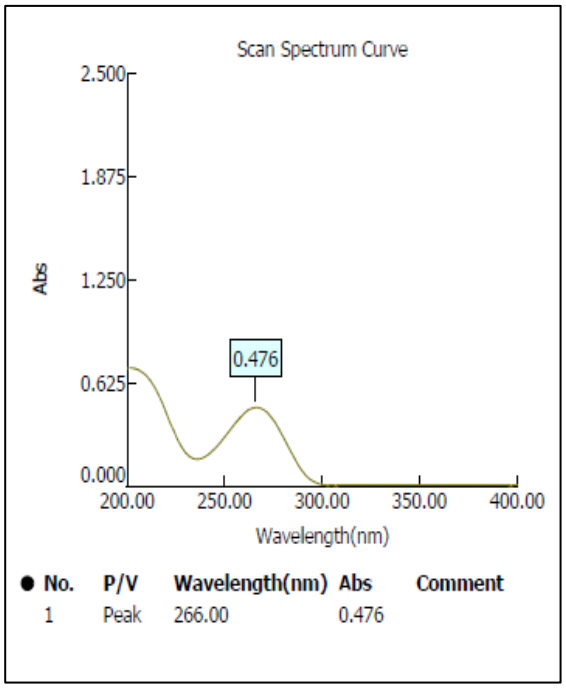


Figure 2: UV Spectrum of Zidovudine

Evaluation of tablets:

Hardness

The test was done as per the standard method. The hardness of three randomly selected tablets from each formulation (F1 to F9) was determined by placing each tablet diagonally between the two plungers of tablet hardness tester (with the nozzle) and applying pressure until the tablet broke down into two parts completely and the reading on the scale was noted down in Kg/cm^2 . The results are presented in Table 3.

Thickness

The thickness of three randomly selected tablets from each formulation was determined in mm using vernier caliper. The average values were calculated. The results are presented in Table 3.

Weight variation

Weight variation test was done as per standard procedure. Twenty tablets from each formulation (F1 to F9) were weighed using an electronic balance and the average weight was calculated. The average weight of one tablet is determined from the collective weight and find out % variation as per table. The results are shown in Table 3.

Table 2: Weight variation of tablets (IP 2007)

Average weight of tablets (mg)	Maximum % difference allowed
80 or less	10
80 – 250	7.5
More than 250	5

Friability

The friability of tablets was measured using a Veego Friablator. Tablets were rotated at 25 rpm for 4 minutes or up to 100 revolutions. The tablets were taken out, dedusted and

reweighed. The percentage friability was calculated from the loss in weight as given in equation below. The weight loss should not more than 1%.

The results are shown in Table 3.

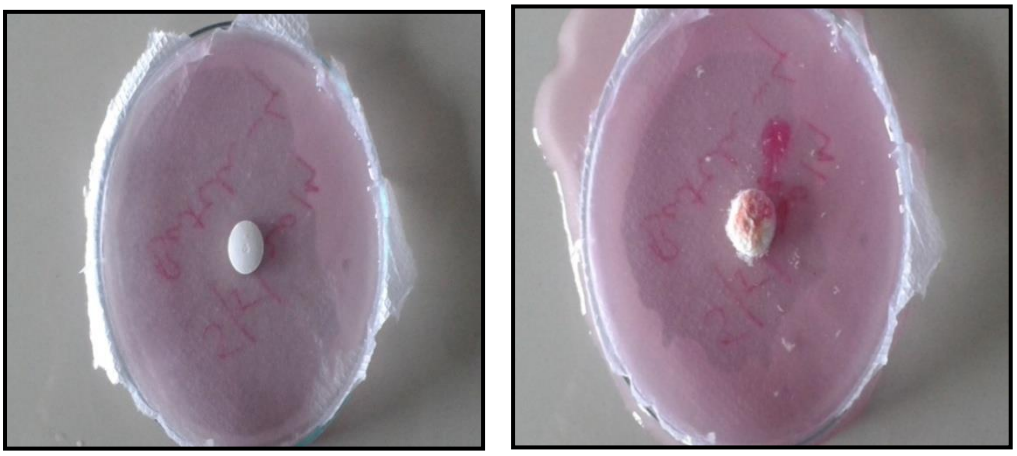
$$\% \text{ Friability} = \frac{(\text{Initial weight} - \text{Final weight}) \times 100}{(\text{Initial weight})}$$

Drug content

Ten tablets from each batch were finely powdered and the powder equivalent to 5mg of Zidovudine was weighed and dissolved in suitable quantity of methanol. the solution was filtered, suitably diluted and the drug content was analyzed spectrophotometrically at 266nm.

Wetting time

The tablet was placed at the centre of two layers of absorbent paper fitted into a dish. After the paper was thoroughly wetted with saline phosphate buffer (pH-6.8), excess water was completely drained out of the dish. The time required for the water to diffuse from the wetted absorbent paper throughout the entire tablet was then recorded using a stopwatch. The results are presented in Table 4 and Figure 3.



(a) (b)

(a) = Before Wetting, (b) = After Wetting
Figure 3: Wetting Time of Zidovudine MDT

Water absorption ration

A piece of tissue paper folded twice was placed in a small petri dish containing 6 ml of saline phosphate buffer (pH- 6.8). A tablet was put on the tissue paper and allowed to completely wet. The wetted tablet was then weighted. Water absorption ratio, R was determined using following equation. The results are presented in Table 5 and Figure 2.

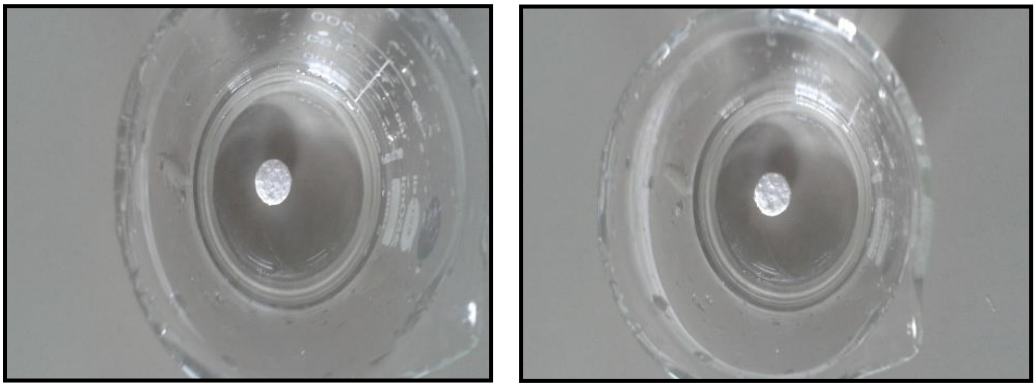
R = Wa-Wb/Wax 100

Where, Wa = weight of tablet after water absorption

Wb = Weight of tablet before water absorption

In- vitro Disintegration test

Tablet was added to 10 ml of phosphate buffer pH 6.8 and time required for complete dispersion was measured (Figure 4). Three tablets from each formulation were randomly selected and in vitro disintegration time was performed.



(a) (b)

(c)

(a)- Before disintegration and (b, c) - After disintegration

Figure 4: In- vitro Disintegration Time Study of Zidovudine MDT

In- vitro Dissolution test

In vitro dissolution studies for all the fabricated tablets was carried out using dissolution apparatus (Electrolab TDT-8L) USP paddle method at 50 rpm in 900 ml of phosphate buffer pH 6.8 as dissolution media, maintained at 37±0.5°c. 5ml sample of the solution was withdrawn from the dissolution apparatus at 5, 10, and 15 min. The samples were replaced with fresh dissolution medium of same quantity. The samples were filtered through Whattman filter paper and analyzed by UV spectrophotometer at 266nm . The percentage drug release was calculated using an equation obtained from the calibration curve. The results are presented in Table 5 and Figure 5, 6, 7..

RESULTS AND DISCUSSIONS:

The powder blend for all the formulation containing various concentrations of superdisintegrant (sodium starch glycolate and crosscarmellose sodium) and direct compressible material such as microcrystalline cellulose were used. The Zidovudine mouth dissolving tablets were prepared by direct compression method using R and D tablet press punching machine by Cemach Pvt. Ltd. The tablets were evaluated for weight variation, hardness, thickness, friability, drug content, water absorption ratio, wetting time, In-vitro disintegration time and In-vitro dissolution rate.

It was observed that all the tablets from each formulation passed the test for weight variation, as the percentage of weight variation was within the pharmacopoeial limits. The weight variation in all formulations (F1 to F9) was found to be in the range of 500 mg to 489 mg, which was within acceptable limits.

The prepared tablets in all formulations possessed good mechanical strength with sufficient hardness in the range of 3.2 to 3.6 kg/cm^2. The tablet mean thickness was almost uniform on all formulations. The thickness varies between 3.1 to 3.2 mm. The friability varies between 0.48 to 0.52 %. The friability values between 1% were an indication of good mechanical resistance of tablet. The drug content in all formulations (F1 to F9) was highly uniform and in the range of 99.03 to 100.06 %. The wetting time was found in the range of 17 to 20 sec. The water absorption ratio in all the formulations (F1 to F9) was found to be in the range of 96.1 to 102.2 %. The disintegration time in all formulations were observed within fraction of seconds. The disintegration time in all formulations (F1 to F9) was found to be in the range of 19 to 25 sec. The in-vitro dissolution studies of all formulations (F1 to F9) were conducted and the results are shown in Table 5 and Figure 5, 6, 7.

Table 3: Weight variation, Hardness, Thickness and Friability of Zidovudine MDT

Batch	Weight variation	Hardness(kg/cm^2	Thickness(mm)	Friability (%)
F1	497.30±0.12	3.1±0.3	3.2±0.02	0.48±0.02
F2	489.20±0.34	3.2±0.6	3.3±0.03	0.52±0.03
F3	499.54±0.43	3.2±0.4	3.2±0.02	0.51±0.01
F4	500.10±0.12	3.2±0.7	3.2±0.02	0.49±0.02
F5	498.30±0.21	3.3±0.2	3.2±0.02	O.48±0.02
F6	499.23±0.24	3.1±0.1	3.2±0.01	O.50±0.06
F7	500.08±0.45	3.2±0.3	3.1±0.02	0.51±0.03
F8	497.75±o.56	3.3±0.4	3.2±0.01	0.50±0.02
F9	499.88±0.24	3.2±0.2	3.1±0.01	0.51±0.02

*values are Mean value of 3 observations

Table 4: Water absorption ratio, Wetting time, Disintegration time, and Drug content of Zidovudine MDT

Batch	Water absorption ratio (%)	Wetting time(sec)	Disintegration time(sec)	Drug content (%)
F1	96.1±0.10	19±1	25±1	99.07±0.93
F2	97.3±0.60	20±2	24±1	100.01±0.67
F3	98.2±0.57	19±3	24±3	100.1±0.87
F4	100.1±0.36	20±2	21±2	99.05±0.57
F5	97.2±0.22	17±2	20±2	100.06±0.34
F6	100.3±0.30	19±1	19±1	100.01±0.48
F7	102.2±0.40	19±3	20±1	99.03±0.92
F8	100.1±0.32	18±2	21±3	99.08±0.98
F9	101.2±0.56	18±4	22±2	100.01±0.99

*values are Mean value of 3 observations

Table 5: % Drug release of Tizanidine Hydrochloride formulation F1-F9

Formulation code	Cumulative % Drug Release			
	0min	**5min**	**10min**	**15min**
F1	0.00±0.00	70.30±0.22	82.10±0.32	98.95±0.14
F2	0.00±0.00	83.40±0.21	85.31±0.13	100.34±0.10
F3	0.00±0.00	79.98±0.17	83.93±0.25	99.20±0.10
F4	0.00±0.00	75.21±0.20	81.23±0.09	96.90±0.13
F5	0.00±0.00	78.18±0.09	84.12±0.15	98.89±0.23
F6	0.00±0.00	80.26±0.27	96.93±0.10	100.10±0.18
F7	0.00±0.00	67.40±0.08	83.23±0.14	98.13±0.19
F8	0.00±0.00	75.45±0.50	84.70±0.33	99.20±0.18
F9	0.00±0.00	74.21±0.32	80.11±0.41	97.14±0.20

*values are Mean value of 3 observations

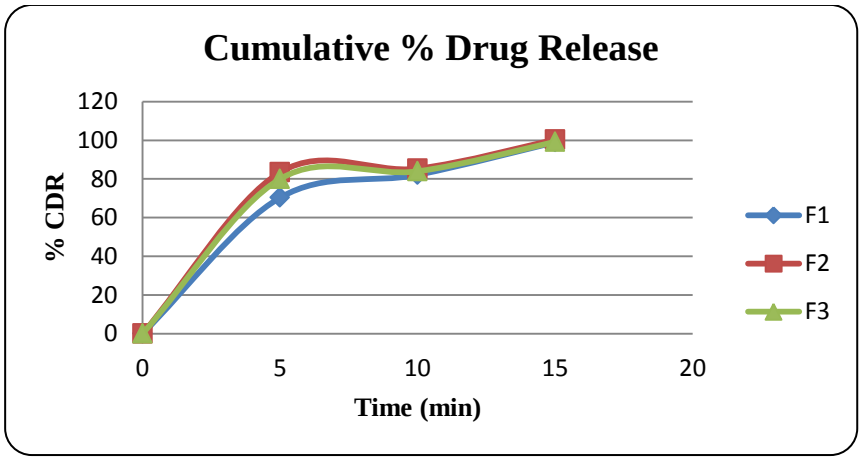


Figure 5: Cumulative % Drug Release of Zidovudine MDT Formulation F1, F2, F3

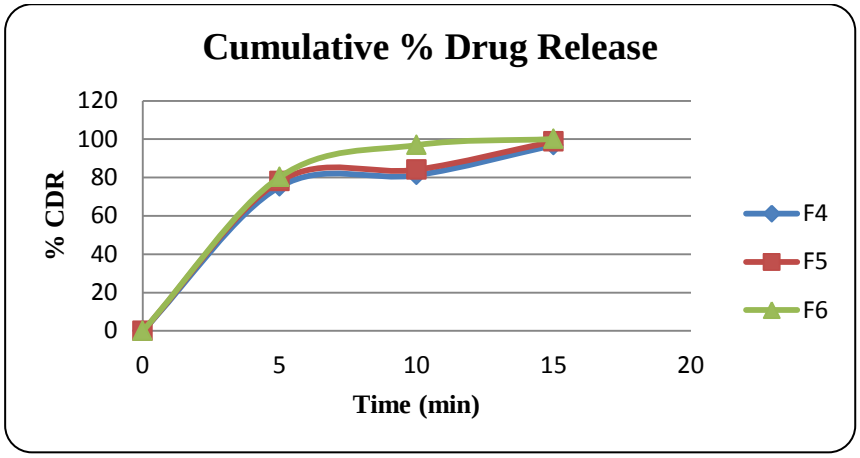


Figure 6: Cumulative % Drug Release of Zidovudine MDT Formulation F4, F5, F6

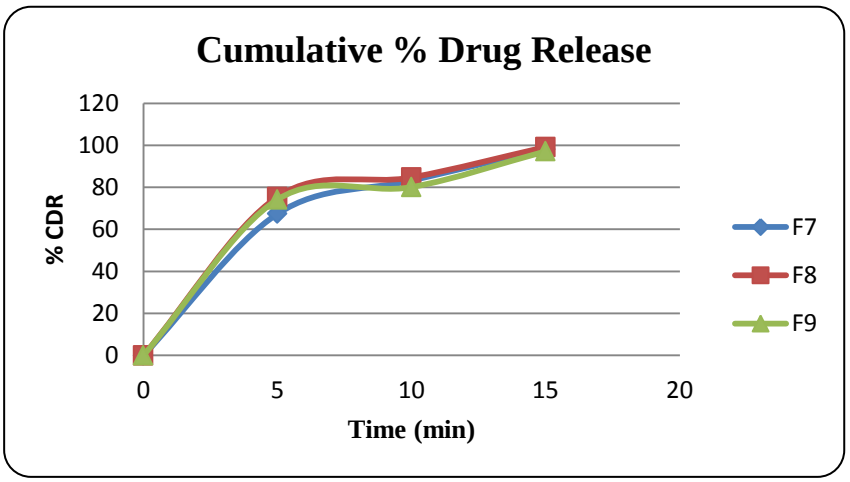


Figure 7: Cumulative % Drug Release of Zidovudine MDT Formulation F7, F8, F9

CONCLUSION:

In present studies, it may be concluded that the mouth dissolving tablets of Zidovudine can be prepared by direct compression using superdisintegrants. Among all the formulations (F1 to F9) the F6 formulation was found to be the best formulation in which combination of superdisintegrants (Sodium starch glycolate and Crosscarmellose sodium) was used in 1:1 proportion (5%, 5%). This formulation showed the least disintegration time of 19.1 sec and the highest release of more than 99% of drug in 15 minute.

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