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## RESEARCH ARTICLE

**FORMULATION DEVELOPMENT AND RELEASE STUDIES OF ZIDOVUDINE SUPPOSITORIES****N Santhi Priya\*, CH Swaroop Reddy, CH Gowtham Sai, G Madhusudana Rao, G Lakshman Reddy, M Santhosh Aruna**

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**ABSTRACT:**

The present manuscript deals with the study to formulate and evaluate suppository for the successful delivery of Zidovudine through rectal administration. Zidovudine has tendency to cause gastric ulcer making it necessary to explore safer routes of its administration. Melt Fusion method was used for the preparation of suppositories using glycerogelatin and Emulsified glycerogelatin as suppository base. The prepared suppositories were evaluated for their visual characteristics, physicochemical properties like dimensions, weight variation, melting time, disintegration time, drug content and *in-vitro* drug release characteristics. The release was found to be greater in emulsified suppositories with satisfactory disintegration time.

Keywords: suppository, Fusion method, Zidovudine

**I. INTRODUCTION:**

In the recent years a logic treatment alternative for the patients who cannot tolerate the oral administration has been utilized for the concurrent minimization of the gastro intestinal disorders caused by local anesthetics, anti haemorrhoidal agents, anti anemic agents, anti fungal and anti bacterial agents, anti asthmatic agents, anti psychotic agents and a majority of the natural and synthetic drugs. Rectal route of administration is especially used for infants and children who have the difficulty in swallowing the dosage forms through oral route.<sup>1</sup>

A suppository is a medicated solid dosage form generally intended for use in the rectum, vagina, and to lesser extent, the urethra. Rectal and urethral suppositories usually employ vehicles that melt or soften at body temperature, whereas vaginal suppositories sometimes called pessaries are also made as compressed tablets that disintegrate in the body fluids.<sup>2</sup> Bases act as the vehicles or carriers of drugs. A variety of substances has been used as suppository bases from the commencement of the history of suppository. Their use was governed by the factor of their availability rather than scientific approach. These bases play an important role in the release of medication they hold and therefore the availability of drug.

Zidovudine (ZDV), is an important drug used for the treatment of HIV infection. It belongs to the family

of nucleoside analogue reverse transcriptase inhibitors (NRTIs). The effectiveness of ZDV in the treatment of HIV infection is due to its selective affinity for HIV reverse transcriptase as opposed to human DNA polymerases. Since HIV is capable of mutating and thus of developing resistance to the drug, Zidovudine is an FDA approved drug for clinical use in the treatment of adults and children with HIV infections or in combination with other anti-viral agents. This drug is typically administered in the form of tablets, capsules and an oral solution. The drug has a short half-life of about 3 hours and it necessitates frequent administration. In order to overcome drug resistance the present research work deals with the development of suppositories by incorporating zidovudine.

**II. MATERIALS AND METHODS :**

**1. Materials:** Zidovudine was procured as a gift sample from Hetero Labs, Hyderabad. All other chemicals and solvents were of analytical grade and used as procured.

**2. Experimental methodology:****A] Calibration of the suppository mould: <sup>4</sup>**

Mould calibration was performed. Each mould of 1 gm capacity was calibrated before the actual preparation by a set of blank suppositories containing the molten base alone. The product is weighed and the mean weight is taken as the true capacity of the suppository mould. The

calibration procedure is repeated before every suppository formulations preparation. The calibrated mould capacities ranged from 1to2gms.

### B] Preparation of suppositories: <sup>5</sup>

**Melt Fusion method:** Drug displacement values of the bases used were first determined and the amount of drug required was calculated. The drug powder was passed through a mesh sieve of 100 µm prior to its incorporation into the base. This method involves first

melting the suppository base, and then dispersing or dissolving the drug in the melted base. The mixture is removed from the heat and poured into a prelubricated suppository mold. When the mixture has congealed, the suppositories are removed from the mold. Tween-80 was incorporated in the formulation to enhance the release of the drug from the formulation. The compositions of the formulation batches were given in the table 1

**Table1: Formulation table of zidovudine suppositories (All values are in percentages)**

S.N	INGREDIENTS	F1	F2	F3	F4	F5
1	Zidovudine	1	1	1	1	1
2	Glycerin	70	60	50	70	70
3	Gelatin	10	10	10	10	10
4	Purified water	20	20	20	20	20
5	Tween80	-	-	-	1	2

### C] Evaluation of zidovudine suppositories:

**Physical Dimension<sup>7</sup>** The width and length of randomly selected suppositories were measured.

**Weight Uniformity** About 20 suppositories were taken and the average weight was determined. Not more than two individual suppositories should deviated by 10%.

**Crushing Strength<sup>9</sup>** The crushing strength was determined for measuring fragility or brittleness of suppositories, which assessed the suppositories whether they would be able to withstand the hazards of packing, transporting and normal handling are not.

### Drug Content Uniformity<sup>10</sup>

Uniformity of drug content was confirmed by analyzing the drug content in equal batch after dissolving the suppositories in 0.1N NaOH and the drug content was determined at 450 nm.

The results were tabulated in Table-3

### In Vitro Drug Release Studies <sup>6</sup>

The dissolution of Zidovudine was studied the using USPXXI dissolution apparatus employing basket stirrer. Zidovudine suppositories were placed dissolution medium contain 0.1N NaOH solution. The rpm was adjusted to 50 and a temperature of 37°C was maintained throughout the experiment. A 5 ml of sample was withdrawn at various time intervals and diluted with 0.1N NaOH The volume of the dissolution medium was kept constant by replacing the withdrawn volume of the sample with equal volume of fresh dissolution medium maintained at the same temperature. A minimum of triplicate release rate determinations were made for each suppository preparation. and analyzed using UV spectrometer. The results of the drug release were given in Table-4

## III. RESULTS AND DISCUSSION:

Vaginal suppositories of zidovudine, an antiretroviral drug, were prepared by fusion method using Glycero-

gelatin and emulsified glycerogelatin as bases .The prepared suppositories were evaluated for appearance, weight variation ,drug content uniformity, liquefaction/softening time, invitro dissolution. The previously calibrated moulds (1gm capacity)were used for the preparation. The calibrated mould capacities displacement values ranged from 0.95 to 1.02g.All the suppositories were free from cracks and fissures by appearance. All the longitudinal sections of the suppositories were identified clear and plain. Also the prepared suppositories were evaluated for weight uniformity and the results are given in table. The percentage deviations from the mean weights of all batches were found to be within the prescribed limits (mean weight  $\pm 5$ to $\pm 7.5\%$ ) as per Indian pharmacopoeia. The drug content was found to be in the range of 97 to 99%.This was also found to be within the limits. The standard deviation values indicated uniform drug content present within the prepared suppositories. The softening time is the time for which the suppositories withstand the body temperature at 37°C.The disintegration range was observed to be 4 to 5 min, but the emulsified medicated suppositories exhibits no liquefaction at that temperature. Invitro dissolution studies on the designed formulations were carried out in pH7.4 phosphate buffer and the various dissolution parameters were determined. The results obtained are shown in Table and the dissolution profiles were shown in figures. The data reveals that Glycero-gelatin suppositories(F1-F3 released zidovudine upto 83-87% and the emulsified glycerogelatin suppositories(F4-F5) released the drug upto 90%.As the emulsifier concentration is increased the drug release was decreased in emulsified glycerogelatin suppositories whereas in glycerogelatin suppositories the drug release was decreased by the increase of glycerin composition ,in case the release rate decreases because of the high molecular weight and the complex polymer structure of gelatin.

**Table 3: Physicochemical evaluation of suppositories**

Formulation Code	Crushing strength(gm)	Drug content %±SD	Weight uniformity(gm)	Physical length(cm)	Dimension width(cm)	Disintegration time(min)
F1	500±0.18	97.99±0.89	0.850	1.813	0.890	4.08
F2	150±0.23	98.56±0.12	0.858	1.811	0.888	5.07
F3	250±0.45	99.64±0.88	0.844	1.813	0.889	5.00
F4	450±0.24	99.89±0.74	0.852	1.814	0.898	5.62
F5	500±0.21	99.06±0.15	0.700	1.814	0.899	4.89

**Table4: Drug release profile of zidovudine suppositories**

TIME	% DRUG RELEASED				
	F1	F2	F3	F4	F5
5	48.84	45.5	42.15	40.48	49.05
10	65.57	53.86	58.86	50.52	52.21
15	67.24	65.57	65.58	65.27	68.55
30	68.92	70.50	67.24	67.24	70.25
45	72.96	75.61	68.92	70.50	75.52
60	75.52	77.28	75.21	72.26	79.44
90	83.92	80.63	82.30	85.30	85.69
120	83.91	84.23	84.21	87.52	90.45

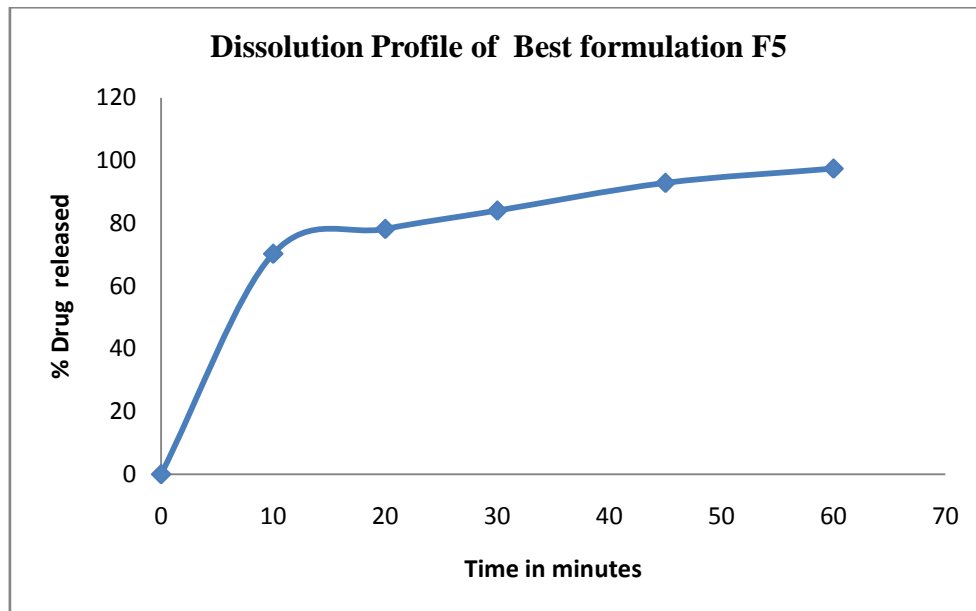


Figure 1: Dissolution Profile of Best formulation F5

**IV. CONCLUSION:**

The present study indicates that it is possible to design vaginal suppositories for the drug Zidovudine, employing the water soluble polymeric base like Glycero-gelatin base. Also this study identifies that by the addition of emulsifiers the drug release profile was modified when compared to Non-emulsified Zidovudine Suppositories. The drug release is nearly first order. However, this study needs In vivo studies in

the animal models to ascertain the relative bioavailability of zidovudine suppositories as a promising platform as dosage form.

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