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Studies on Formulations and Design of Zidovudine Loaded Particulated Vaginal Bioadhesive Tablet

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Abstract: Zidovudine is an antiretroviral drug and used in the treatment of AIDS. The intention of this study was to prepare zidovudine loaded microencapsulated bioadhesive tablets for sustained drug delivery through vagina and to evaluate and elect the best formulation. The micorcapsules of Zidovudine were prepared by solvent evaporation method in different ratios (1:2-1:7), then evaluated to select the best microencapsuleted formulation. The microcapsule formulation selected was then incorporated in tablet by direct compression method using various grades of bioadhesive polymers such as carbapol-934, carbapol-940, sodium carboxy ethyl cellulose and sodium alginate. The prepared tablets (F1 to F12) were subjected to various evaluations .Zidovudine release from the tablet formulations were slow and sustained over longer period of time. Among all formulations batch containing carbapol-934(1:1) was found to be the best optimized microencapsulate vaginal bioadhesive tablet formulation with regards to practical drug content, swelling index, bioadhesive strength study as well as sustained drug release property.
Key words: Zidovudine, microparticulates, bioadhesive tablet.

INTRODUCTION

For many decades treatment of an acute or a chronic illness has been mostly accomplished by delivery of drugs to patients using conventional dosage form due to patient compliance and acceptability. [1] The traditional oral dosage form has a certain disadvantages that needed to be overcome such as short retention tie in GIT. [2] The goal of noble drug delivery system is to achieve therapeutic concentration of a drug at the target site quickly and then maintain the desired concentration at the site for a specific period of time. [1]

Conventional vaginal formulation, associated with disadvantage of low retention to the vaginal epithelium, leakage and messiness thereby causing inconvenience to the user. To circumvent this problem, bioadhesive drug delivery systems are being propagated. Bioadhesive polymer that have been used for vaginal formulation include polycarbophil, hydroxypropyl cellulose and polyacrylic acid. A bioadhesive polycarbophil gel Replens is available in the market, which, used to retain moisture and lubricate vagina. The formulation remains in the vagina for 2-3 days and maintain the vagina at healthy, acidic pH. Various peptide protein drugs have also been attempted to administer via bioadhesive microparticulate vaginal delivery system. Assemblies for in vitro measurement of bioadhesive strength and

retention characteristics of a polymer in a vaginal delivery system have been reported. A modified simulated vaginal fluid, used to simulate vaginal condition for Bioadhesion. The principle of Bioadhesion is based on the measurement of tensile strength of shear stress required to break the adhesive bond between a model membrane and test formulation.[3, 4]

The main objective of study was to developed and established of microparticulate bioadhesive vaginal tablet for sustained release of drug for local and systemic delivery of Zidovudine , and to overcome leakage problem of conventional dosage forms.

MATERIALS AND METHODS

MATERIALS:-

Zidovudine (Pure grade) was received as a gift sample from Apl Research center (A division of Aurobindo pharma Ltd) A.P, India, Ethyl cellulose(analytical grade) was purchased from Sd-Fine chemicals, Mumbai, Hydroxy propyl methyl cellulose, Carbopol, Sodium carboxy methyl cellulose, Sodium alginate(commercial grade) was purchased from LOBA chemicals pvt ltd, Kolkata, Mg-stearate, Sodium acetate, Trichloro acetic acid (TCA) was procured from Sd-Fine chemicals, Mumbai.All other chemicals used are analytical

PREPARATION OF MICROCAPSULES:

Solvent Evaporation Method: [5, 6]

Zidovudine (AZT) microcapsules were prepared by the solvent evaporation method. Accurately weighed quantities of polymer were dissolved in acetone (20ml). The drug and polymer (1:2 - 1:7) ratios were dissolved or dispersed in acetone and added to light liquid paraffin with continuous stirring (1000 rpm). Stirring is continuing for 3 hrs. Microcapsules were recovered by treating with petroleum ether, then filtered, dried and kept in desiccators for further evaluations. The code of the microcapsule is given as MC2 (1:2), MC3 (1:3), MC4 (1:4), MC5 (1:5), MC6 (1:6), and MC7 (1:7).

EVALUATION OF MICROCAPSULES:

Percentage Yield [7]

The yield was calculated as the weight of the microcapsules recovered from each batch divided by total weight of drug and polymer used to prepare that batch multiplied by 100.

Drug Content and Drug Encapsulation efficiency (DEE) [8]

Accurately weighed amount of microcapsules 100 mg, were suspended in 50ml of methanol to dissolve the polymer coat. The drug was extracted with 50 ml of methanol in separating funnel and analyzed by using UV-Visible spectrophotometer (UV-1700, Shimadzu, Japan) 267nm after suitable dilution . The drug entrapment efficiency (DEE) was calculated by the following equation3 DEE = (Pc / Tc) X 100 where Pc is practical drug content; Tc is the theoretical drug content. The entire test was performed in triplicate.

Micromeritic Studies [.9-11]

Flow of microcapsules was investigated by determining angle of repose, bulk density, Carr's index and Hausner ratio. The angle of repose was determined by fixed funnel method. The microcapsules were tapped using bulk density apparatus (Excel Enterprises, Kolkata) for 100 taps in a cylinder and the change in volume was measured. Carr's index and Hausner ratio were calculated by the formula: Carr's index (%) = [(Df -D0) ×100] / Df and Hausner ratio = Df / D0, Where, Df is tapped density; D0 is poured density. All the experimental units were studied in triplicate (n=3).

Morphological and Size Distribution Characterization [12]

Microcapsules were observed and photographed with scanning electron microscopy (SEM) (LEO, 435 VP, U.K.) and optical microscopy (OLYMPUS BX-50, Japan).

***In-Vitro* Drug Release Study** [13]

In vitro drug release study was carried out in USP type II dissolution test apparatus using SVF (simulated vaginal fluid) as dissolution medium (900 ml acetate buffer I.P. pH 4.7, at 37±1 °C, Peddle speed was adjusted to 50 rpm. An aliquot sample (5 ml) was withdrawn
at intervals of 1 h with replacement by fresh medium and analyzed for Zidovudine content by UV-Visible spectrophotometer at 267 nm. The entire release tests were performed in triplicate.

***In Vitro* Drug Release Kinetic Study** [14]

In order to study the exact mechanism of drug release from the Vaginal Microcapsules, drug release data was analyzed according to zero order, first order, Higuchi square root and Korsmeyer – Peppas equations. The criterion for selecting the most appropriate model was chosen on the basis of goodness of fit test.

Fourier Transformed Infrared spectroscopy [15]

IR spectroscopy was performed on Fourier transformed infrared spectrophotometer (840, Shimadzu, Japan). The pellets of drug and potassium bromide were prepared by compressing the powders at 20 psi for 10 min on KBr-press and 2mg of pure drug, empty microcapsules and drug loaded microcapsules were selected and measured in the range the spectra

were scanned in the wave number range of 3000-400 cm^{-1}.

PREPARATION OF MICROENCAPSULATED BIOADHESIVE TABLET [16-18]

Selected batches of Zidovudine microcapsule (MC4) were incorporated in tablet by direct compression method using various grades of bioadhesive polymer, such as Carbopol 934, Carbopol 940, Sodium Carboxy Methyl Cellulose, Sodium Alginate with other formulation excipients. For all batches, the microcapsules were mixed with bioadhesive polymer and other formulation additives of tablet as designed in table 8 and 9.

EVALUATION OF MICROENCAPSULATED BIOADHESIVE TABLET:

Determination of the Weight Variation of the Tablets [19]

Twenty tablets were selected at random from each batch and were weighed accurately and the average weight was calculated. Then the deviation of individual weights from the average weight and the standard deviation was calculated.

Determination of Hardness of the Tablets [19.20]

Five tablets were sampled randomly selected from each batch and the hardness of the tablets was determined by the help of the Monsanto Hardness Tester. Then average hardness and standard deviation was calculated.

Determination of Friability of Tablets [19, 20]

The friability test was done using Roche's friabilator. Twenty tablets were selected and weighed individually. Then the friability test was carried out at 25 rpm for 4 minutes. These tablets were then again weighed and percentage loss in weight was calculated.

Determination of Thickness and Diameter [19]

Thickness and Diameter of five randomly selected tablets from each batch were measured with a slide caliper scale. Then the average diameter and thickness and standard deviation were calculated. Tablet thickness should be controlled within 5% variation of a standard value.

Determination of Disintegration Time of Tablets [21]

Vaginal tablets place the apparatus in a vessel of suitable diameter containing water at 36° to 37°C. Adjust the level of the liquid by the gradual addition of water at 36° to 37° until the perforations in the metal disc are just covered by a uniform layer of water. Place one vaginal tablet on the upper perforated disc and cover the apparatus with a glass plate to maintain appropriate conditions of humidity. Repeat the operation with a further two vaginal tablets.

Disintegration is considered to be achieved when

(a) There is no residue on the perforated plate or
(b) If a residue remains, it consist only a soft or frothy mass having no solid core offering resistance to pressure with a glass rod.

Determination of Practical Drug Content [22]

Three tablets were chosen randomly from each of the formulation and taken separately into three 100 ml volumetric flask. In each flask 100 ml of acetate buffer pH 4.7 was kept for 24 hr. After filtration the solution, the absorbance of the filtrate was measured in UV visible spectrophotometer at 267 nm.

***In vitro* Dissolution Study of the Drug** [22]

In-vitro drug release study from bioadhesive tablet was carried out using USP XXII peddle type dissolution test apparatus using acetate buffer pH 4.7 as dissolution medium. Volume of dissolution medium was 900 ml and bath temperature was maintained at 37±0.5°C throughout study period. The rotating rate of the peddle was adjusted to 50 rpm. At The absorbance values of the sample were measured by UV-Visible spectrophotometer at the wavelength of 267 nm.

***In vitro* Drug Release Kinetic Study** [14]

To elucidate kinetics of drug release from the prepared bioadhesive tablet, the data was analyzed according to different kinetic equations viz. zero order, First order, and Higuchi kinetic model.

Bioadhesive Strength of Tablets: [22]

The bioadhesive measurement was performed by using a modified balance method intact with mucosal membrane of goat vagina in vitro as reported by Sanjay garg et al for tablet bioadhesion measurement.

Swelling Index of Tablets: [21]

The weight of medicated tablets was determined (W_1). Each tablet was placed separately in a glass petridish containing 5 ml acetate buffer pH 4.7. The petridish was stored at room temperature. Tablet were removed at different time intervals (20min, 40min, 1hr, 2hr, 4hr) wiped with butter paper, and reweighed (W_2) of the tablet. The swelling index was calculated as follows

Swelling index= $(W_2-W_1)/W_1$

Table 1 composition, % yield, drug content, DEE and flow properties of vaginal microcapsules

Formu -lation code	Drug/ polyme r ratio	% yield	Drug Content (mg)	Encapsulation efficiency (%)	Carr' Index	Hausner's ratio	Angle of Repose (°)	Comment
MC2	1:2	79.10±0.39	19.31±0.73	45.83±1.62	13.20	1.19	21.08	Good
MC3	1:3	76.33±0.21	18.27±0.28	55.78±0.97	10.42	1.20	17.54	excellent
MC4	1:4	84.26±0.17	23.35±0.19	98.34±0.93	9.83	1.13	19.80	excellent
MC5	1:5	60.16±0.19	14.14±0.52	51.07±1.91	10.11	1.26	27.21	Good
MC6	!:6	92.52±0.12	8.10±0.04	52.48±0.34	17.41	1.29	18.14	excellent
MC7	1:7	87.74±0.25	13.17±0.15	92.48±1.24	14.31	1.11	23.87	Good

***All the results are expressed Mean ± SEM (n=3).**

Table 2 *In Vitro* Drug Release Kinetic Studies of Zidovudine Loaded Microcapsule formulations.

FC	Zero order		First order		Higuchi model		Korsmeyer-peppas model		
	r^2	Ko (µg/sec)	r^2	K_1	r^2	K_H (µg/√sec)	r^2	n	comment
MC2	0.557	2.704	0.946	-0.046	0.788	15.46	0.993	0.182	Fickian diffusion
MC3	0.530	2.036	0.750	-0.019	0.858	11.71	0.981	0.141	Fickian diffusion
MC4	0.745	1.437	0.756	-0.013	0.976	10.53	0.99	0.172	Fickian diffusion
MC5	0.621	2.275	0.828	-0.020	0.937	12.70	0.982	0.162	Fickian diffusion
MC6	0.826	10.69	0.998	-0.186	0.969	34.70	0.947	0.343	Fickian diffusion
MC7	0.502	2.039	0.730	-0.015	0.762	12.07	0.976	0.225	Fickian diffusion

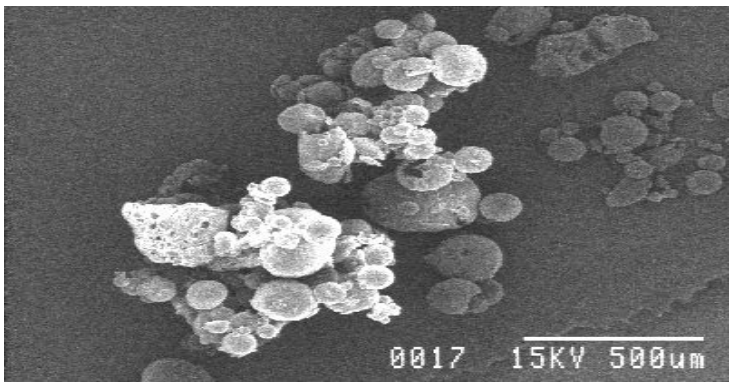


Fig 1 Scanning Electron Micrograph of Microcapsules (MC4) Under Lower Resolution of X 30.

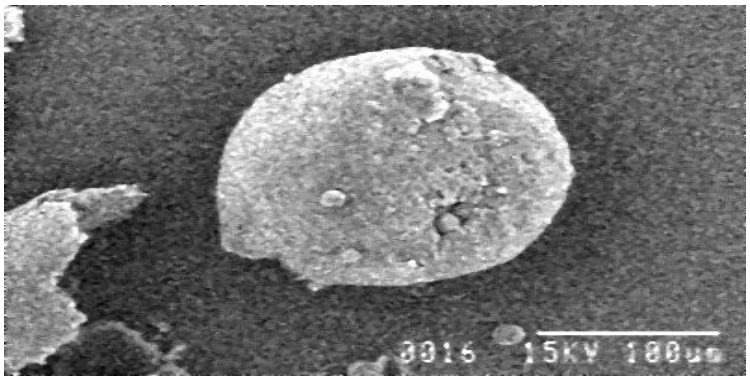


Fig 2 Scanning Electron Micrograph of Microcapsules (MC4) Under Higher Resolution of X 300.

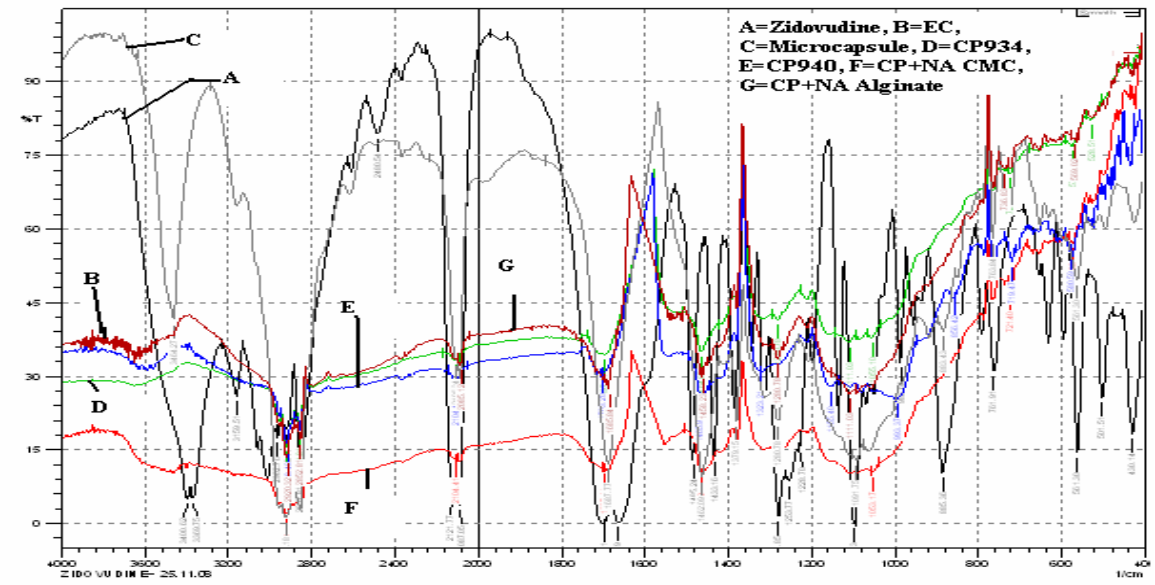


Fig 3 FT-IR Spectra of Pure Drug, Microcapsule Formulation, and Tablet Formulation.

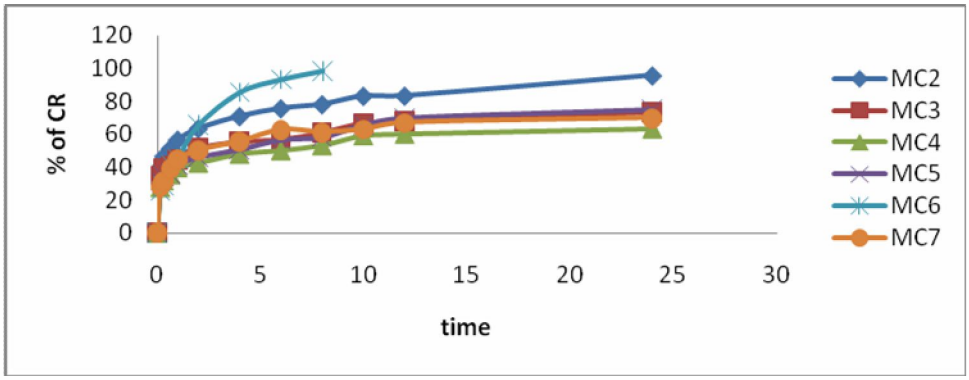


Fig 4 *In Vitro* Zero Order Release Profile of Zidovudine loaded microencapsulated formulations

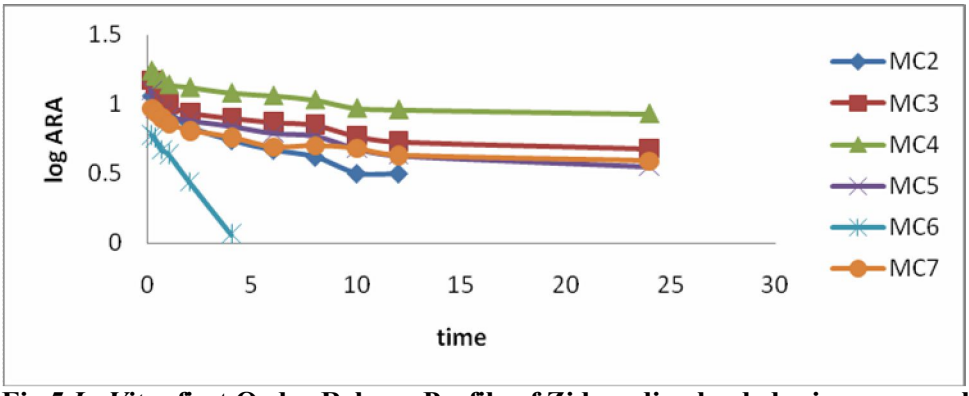


Fig.5 *In Vitro* first Order Release Profile of Zidovudine loaded microencapsulated Formulations

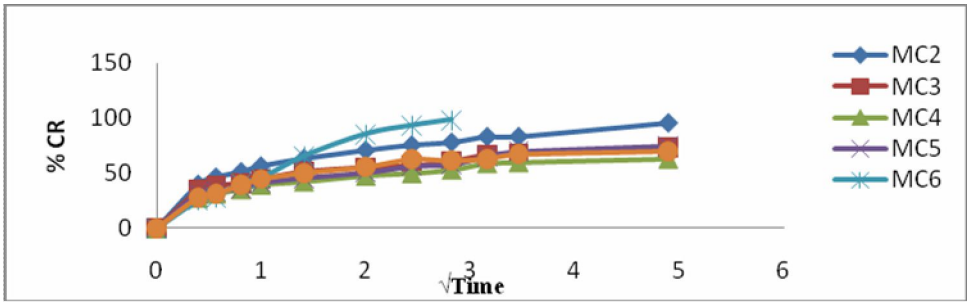


Fig 6 Higuchi Release Kinetics of the Zidovudine loaded microencapsulated Formulations

Table 3 Formulation Design of Microencapsulated Vaginal Bioadhesive Tablets:

FC	MC:Polymer	MC* (mg)	Carbopol-934 (mg)	Carbopol-940 (mg)	Starch (mg)	Mg.stearate (mg)
F1	1:1	101.68	101.68	-	186.64	10
F2	1:1.5	101.68	152.52	-	135.8	10
F3	1:2	101.68	203.36	-	84.96	10
F4	1:1	101.68	-	101.68	186.64	10
F5	1:1.5	101.68	-	152.52	135.8	10
F6	1:2	101.68	-	203.36	84.96	10

Table 4 Formulation Design of Microencapsulated Vaginal Bioadhesive Tablets:

FC	MC* (mg)	Na.CMC : CP-934	Na.Al : CP-934	Na.CMC (mg)	Na.Al (mg)	CP-934 (mg)	Starch (mg)	Mg.stearate (mg)
F7	101.68	1:1	-	125	-	125	38.32	10
F8	101.68	1:2	-	83.34	-	166.66	38.32	10
F9	101.68	1:3	-	62.5	-	187.5	38.32	10
F10	101.68	-	1:1	-	125	125	38.32	10
F11	101.68	-	1:2	-	83.34	166.66	38.32	10
F12	101.68	-	1:3	-	62.5	187.5	38.32	10

FC= Formulation code, MC= Microcapsule, Na.CMC= Sodium Carboxy methyl Cellulose, Na.Al= Sodium alginate, CP= Carbopol, Mg.stearate= Magnesium stearate

*Weight of the microcapsule is equivalent to the 100 mg of drug.

Table 5 Weight variations, Hardness, Friability, Disintegration time, Thickness and Diameter Parameter of Tablets:

FC	Weight uniformity (mg)	Hardness (Kg/cm^2)	Friability (%)	DT Time (hr:min)	Thickness (mm)	Diameter (mm)	Drug content (mg)
F1	398.59±0.31	5.2±0.15	0.001±0.00	0.40	5.1±0.00	10.2±0.01	66.70±0.55
F2	398.83±0.72	5.46±0.02	0.002±0.00	1.20	5.7±0.12	10.6±0.02	61.96±0.68
F3	399.78±0.43	6.23±0.14	0.002±0.01	1.35	4.9±0.01	10.1±0.00	63.7±0.24
F4	400.33±0.23	6±0.11	0.004±0.00	0.10	5.9±0.04	10.6±0.20	57.58±0.40
F5	398.56±0.24	5±0.11	0.005±0.00	0.16	5.4±0.11	10.6±0.06	54.02±0.73
F6	400.10±0.16	5.6±0.1	0.005±0.00	0.8	5.2±0.00	11.2±0.03	52.63±0.19
F7	397.33±0.16	4.76±0.02	0.003±0.00	2.10	4.7±0.05	11.2±0.02	46.92±0.07
F8	401.21±0.2	6±0.06	0.006±0.00	2.45	5.4±0.03	10.4±0.12	49.85±0.14
F9	399.65±0.28	6.25±0.15	0.001±0.00	2.40	5.6±0.05	10.1±0.03	47.35±0.38
F10	399.93±0.44	7.5±0.22	0.003±0.00	3.00	5.8±0.14	10.7±0.04	41.41±0.16
F11	400.21±0.56	7.0±0.01	0.006±0.00	3.15	5.6±0.33	11.1±0.01	54.46±0.93
F12	401.82±0.16	5.5±0.2	0.005±0.00	3.10	5.4±0.15	10.8±0.00	44.93±0.49

***All values are expressed in mean ± SEM (n=3).**

Table 6 *In Vitro* Drug Release Kinetic studies of Zidovudine Loaded Microencapsulated Bioadhesive Tablet Formulations:

FC	Zero order		First order		Higuchi model		Korsmeyer-peppas model		
	r^2	Ko (µg/sec)	r^2	K_1	r^2	K_H (µg/√sec)	r^2	n	Comments
F1	0.833	4.820	0.956	-0.029	0.963	17.24	0.996	0.318	Fickian diffusion
F2	0.818	4.946	0.937	-0.034	0.954	17.77	0.992	0.300	Fickian diffusion
F3	0.815	4.735	0.917	-0.041	0.949	17.00	0.991	0.290	Fickian diffusion
F4	0.799	5.168	0.921	-0.034	0.937	18.63	0.963	0.276	Fickian diffusion
F5	0.800	5.677	0.974	-0.046	0.936	20.43	0.937	0.287	Fickian diffusion
F6	0.791	5.624	0.939	-0.042	0.942	20.42	0.960	0.332	Fickian diffusion
F7	0.812	6.117	0.967	-0.051	0.955	22.07	0.969	0.351	Fickian diffusion
F8	0.751	5.237	0.927	-0.037	0.922	19.31	0.977	0.325	Fickian diffusion
F9	0.803	6.211	0.941	-0.053	0.949	22.47	0.998	0.288	Fickian diffusion
F10	0.840	7.032	0.947	-0.083	0.953	24.92	0.989	0.247	Fickian diffusion
F11	0.782	9.432	0.939	-0.166	0.943	31.05	0.996	0.298	Fickian diffusion
F12	0.793	6.014	0.983	-0.052	0.941	21.79	0.995	0.282	Fickian diffusion

Table 7 Swelling Index Studies of Microencapsulated Bioadhesive Tablets:

Formulation code	Swelling index				
	20 (min)	40 (min)	1 (hr)	2 (hr)	4 (hr)
F1	0.891	1.130	1.365	1.650	*
F2	1.328	1.462	1.677	2.188	3.331
F3	1.588	1.570	1.943	2.411	3.429
F4	0.971	*	*	*	*
F5	*	*	*	*	*
F6	1.456	2.308	2.421	2.671	*
F7	0.915	1.233	1.480	1.761	2.442
F8	1.002	1.298	1.531	1.848	*
F9	0.976	1.247	1.696	2.061	*
F10	0.855	1.166	1.463	1.598	2.573
F11	0.949	1.113	1.405	1.645	2.311
F12	1.039	1.281	1.539	*	*

***Swelling could not be possible to measure.**

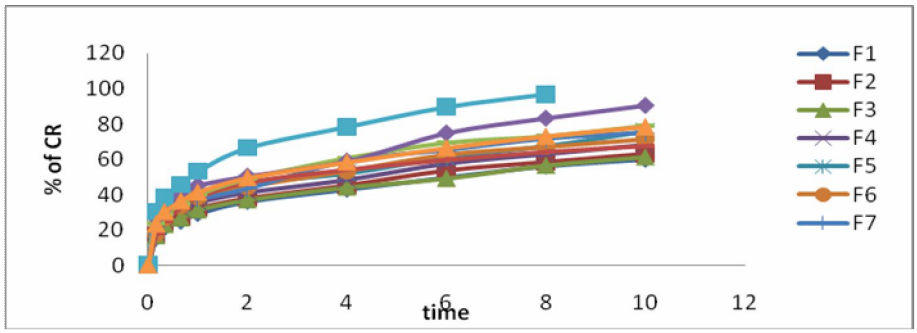
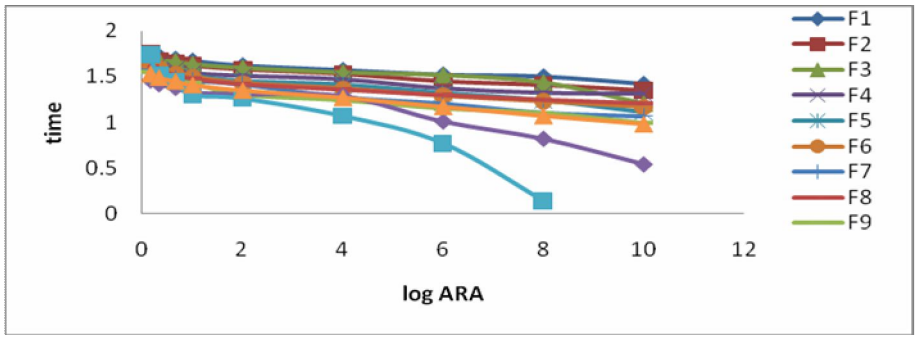


Fig 7 *In Vitro* Zero Order Release Profile of the microencapsulated tablet Formulations



***ARA= Amount remaining to be absorbed.**

Fig 8 *In Vitro* First Order Release Profile of the microencapsulated tablet Formulations

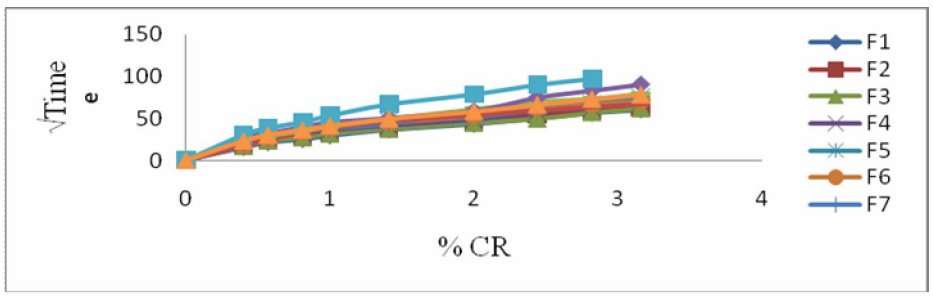


Fig 9 Higuchi Release Kinetics of the microencapsulated tablet Formulations

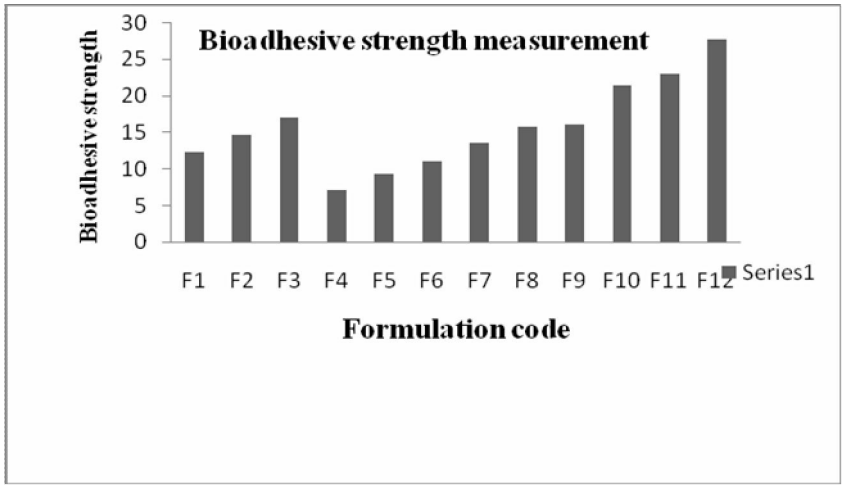


Fig 10 Bioadhesive Strength Measurement of Microencapsulated Bioadhesive Tablets

RESULTS AND DISCUSSIONS

Relatively high 60.16 ± 0.19 to 92.52 ± 0.12 % yield were observed for each formulation presented in column 3 of table 1. The SEM as given in Fig. 1and 2 revealed that all microcapsules thus obtained were opaque, discrete and nearly spherical particles. The particle size of the microcapsules was found to be increased with increase in proportion of coat material as expected. The flow properties of the microcapsules were shown in column 6- 9 of Table 1. As usual, the flow properties increase with polymer ratio. Most of the formulations are having excellent to good flow properties as represented. The drug content found in formulation MC4 is higher and lower drug content was found in formulation MC6 and formulation MC2, MC3, MC5, MC7 drug content was found in less than 20 mg, as shown in column no 4 of table1. Drug entrapment efficiency (DEE) of MC4 and MC7 formulation was found to be high because, the drug solubility in external phase was very less and the drug is fully dispersed in the polymer phase by continuous stirring for a longer period. FTIR studies the characteristics of C-O stretching at around 1095cm^{-1} and-C=O stretching at around 1658 cm^{-1} was clearly distinguished in all the formulation as shown. Additionally peak at 2087 cm^{-1} due to azide group and 3398 cm^{-1} due to O-H stretching were also observed unchanged in all formulation, suggesting no drug polymer chemical interaction as shown in fig 3. All the formulations were found to be release Zidovudine in a sustained manner for a prolonged period over 24 hour and it can be seen that the MC4 shows only 63.36% cumulative drug release over the period of 24^{th} hr where all other formulations give more than 70% drug release in the same period of time. To describe the kinetic of drug release from microcapsule, release data was analyzed according to different kinetic equations. The zero order, First order, and Higuchi model kinetic are described in all microcapsule formulations and abridged in figure no 4, 5 and 6 and table 2. The formulations MC2 and MC6 obey first order kinetic and has dependent on formulation variations. The formulations MC3, MC4, MC5 and MC7 followed Higuchi square root kinetic and have diffusion controlled release rate which is dependent on concentration of release retarding polymer with process variables.

For the selection of final microcapsule formulation, MC4 shows the more sustained drug release characteristic (63.36%) over 24 hr of time as compare to the other formulations. Also MC4 formulation was selected, because it give overall good result of percentage yield, drug content and drug entrapment efficiency study. In Scanning electron microscopy study MC4 formulation also shows that microcapsules obtained were discrete, spherical and uniform in size.

The Zidovudine loaded microencapsulated bioadhesive tablet were prepared by direct compression method by using different polymers in different ratio which are abridged in table 3 and 4. To determine the Weight variation of the formulated tablets was tested in accordance with the procedures given in Indian Pharmacopoeia. Average weight of different formulations was varied from 397.33 to 401.82 which are abridged in table 5. The weight variations of each of the tablet were well within the I.P. limitation (±5%). The hardness of the different formulations was found in the range of 4.7 to 7.5 Kg/cm^2 and is summarized in table 5. Therefore, each of the tablets of the final set of formulation is showing good hardness Properties. The friability test was done using Roche's friabilator. Friability of different tablets varied from 0.001 to 0.006 %. The friability of each of the tablet is well within the I.P. limitation. Disintegration test was carried out according to procedure mentioned in British Pharmacopoeia. Disintegration time of different tablets formulations were found to be in the range of 0.8 min to 3.15 hr which are summarized in

table 5. Tablet formulated with Carbopol-940 (F4, F5 and F6) shows the faster disintegration time where other formulations show long disintegration time. Thickness and Diameter of tablets were measured with a slide caliper scale which is denoted in table 5. The values of the tablet thickness varied from 4.7 to 5.9 mm and diameter range were found in 10.1 to 11.2 mm. All the formulations were found to be release Zidovudine in a controlled manner for a prolonged period over 10 hour and it can be seen that the F1 shows only 60.21% cumulative drug release over the period of 10 hr. Therefore, F1 formulation shows the more sustained and controlled release characteristic when compared to the other formulations. To describe the kinetic of drug release from microencapsulated bioadhesive tablets, release data was analyzed according to different kinetic equations as shown in fig 7-9. The formulations F5, F7, F8 and F12 obey first order kinetic and has dependent on formulation variations. The formulations F1, F2, F3, F4, F6, F9, F10, and F11 followed Higuchi square root kinetic and have diffusion controlled release rate which is dependent on concentration of release retarding polymer with process variables as shown in table 6. The bioadhesive strength of the prepared microencapsulated bioadhesive tablets is measured by using goat vagina. Result of the bioadhesion is denoted in fig 10. In above data formulations F10, F11 and F12 shows the excellent bioadhesive properties compare to the all other formulations. Swelling index plays an important role in the drug release pattern. The swelling index lied in the range of 0.891 to 3.429 as given in table 7. The highest swelling index is achieved in the formulation F3. Values reflect that swelling index was dependent on polymer concentration.

CONCLUSION

Currently, there is a huge interest in the scientific community and drug industry to exploit various mucosal routes of delivering drugs, which are poorly absorbed after oral administration. Although remarkable achievements in AIDS therapy have been attained since this fatal diseases was first recognized more than a decade ago, enormous challenges remain for the researchers to ultimately curb the progression and find a cure for AIDS. Therefore, it can be envisaged that in the near future further studies can be explored using the selected procedures. The future of vaginal drug delivery lies in the bioadhesive tablet, liposome, niosome, and microparticle, which although relatively new but shows great promise in providing truly controlled delivery of drugs. The investigator positively views that in near future these dosage forms will be a reality and can be espoused industrially to deliver Zidovudine in a controlled release fashion for the effective management of AIDS.

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