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RESEARCH ARTICLE

COMPATIBILITY OF ANTI-HIV DRUGS WITH EXCIPIENTS IN THE DEVELOPMENT OF NOVEL TABLET FORMULATION

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Abstract:

The objective of this study to access the compatibility study of Zidovudine with different excipients in the development of sustained release formulation by thermal and FTIR studies. Evaluate the drug excipient compatibility study like differential scanning calorimetry (DSC) and Fourier transform infrared spectrophotometer (FTIR) studies to be performed. the result of DSC study shows that there is no interaction with excipients and the results of FTIR showed that all the excipients were compatible with Zidovudine the optimized formulation. Optimized formulation to be developed with excipients and it was observed the accelerated stability study over 3 months. Overall compatibility study of excipients with zidovudine evaluated and the sustained release formulation developed using compatible excipients were found to be stable.

KeyWords: Zidovudine, sustained release tablets, DSC, FTIR.

INTRODUCTION:

Compatibility of drug excipient represent a important stage of pharmaceutical formulation. Before the formulation in to the specific dosage form, there is need for the formulation scientist to fully consider the chemical structure of the drug substance. the type of delivery system required and the proposed manufacturing process. The drug is mainly combined with excipient which serve different specific purposes [1].

The few reported methods generally used for such studies have poor predictive values and some are laborious and time consuming. Differential scanning calorimetry (DSC) is widely used for evaluating the drug-excipient interaction [2–7]. Exposure of drug-excipient mixture to high temperature (300 °C or more) may deteriorate some of the excipients used.

Zidovudine is active against human immunodeficiency virus (HIV-1&2) which is a retrovirus. Zidovudine is a first antiretroviral drug was developed in 1987. It is useful in prolonging life and postponing complications of acquired immunodeficiency syndrome (AIDS) or AIDS related complex (ARC), but does not cures the infection. The clinical efficacy of antiretroviral drug is monitored primarily by plasma HIV-RNA assays and CD4 lymphocyte count carried out at regular intervals.[8]

In this study it was observed that there is no interaction between two different anti-HIV drug with excipients. So that the prototype formulae of various tablet formulations of anti-HIV drugs can be developed which can be used the production of commercial tablet batch of the drugs. As the prevalence of HIV is a threat to society, this project can be able contribute in the prevention and treatment of the such cases. Hence this project could be very much commercialized and provide better social benefits.

Materials and Methods:

Zidovudine was kindly gift sample from alkem laboratoey, Sikkim, India. Avicel PH 102 purchase form Himedia lab, Mumbai, India. Carbopol974P, Xanthan Gum, Aerosil and Magnesium Stearate was purchased from local vendor.

Differential Scanning Colorimatry:

Differential Scanning Colorimetry Thermogram of pure drug zidovudine, and physical mixture was obtained using a Mettler-Toledo DSC 821e instrument equipped with an intracooler (Mettler-Toledo, Greifensee, Switzerland). Zidovudine standards were used to calibrate the differential scanning calorimetry (DSC) temperature and enthalpy scale. The samples was

hermetically sealed in aluminum pans and heated at a constant rate of 20-C/min, over a temperature range of 0 to 550-C. Inert atmosphere was maintained by purging nitrogen at the flow rate of 100 ml/min.

FTIR studies

The FT-IR spectrum for drugs with excipients was obtained by powder diffuse reflectance on a FT-IR spectrophotometer (Agilent, Cary-2000) in the wave number region of 4000-400 cm-1 to find out drug excipient interaction if any.

Formulation development and stability study of tablets

All ingredients were collected and weighed accurately. Sift Zedovudine USP with Avicel PH 102 and polymers through sieve no. 60# and then rinse with remaining excipients. Sift colloidal silicon dioxide (Aerosil-200) and magnesium stearate separately, through sieve no. 60#. Preblend all ingredients (except lubricant magnesium stearate) in blender for 15 minutes. Add magnesium stearate and then again blend for 5-6 minutes. Lubricated powder was compressed by using rotary tablet punching machine (RIMEK), Ahmedabad). Compressed tablets were examined as per official standards and unofficial tests. Tablets were packaged in well closed light resistance and moisture proof containers.

Table 1: Formulation of Sustained Release Tablet of Zidovudine

Name of Ingredients	Quantity of Ingredients per Tablet (mg)
Zidovudine	300
Avicel PH 102	120
Carbopol974P	50
Xanthan Gum	60
Aerosil	5
Magnesium Stearate	5

The assay of the tablets was carried out as follows. Accurately weighed tablets (n = 6) were dissolved in 100 mL of methanol. The samples were sonicated (Ultra sonic water bath, Loba Chem, India) for 30 min and then filtered through a nylon membrane filter (0.45-µm pore size).

The filtered solution, after appropriate dilution with methanol, was analyzed by a validated UV spectroscopic method [8] at 270 nm (UV-1600, Simadzu, Japan).

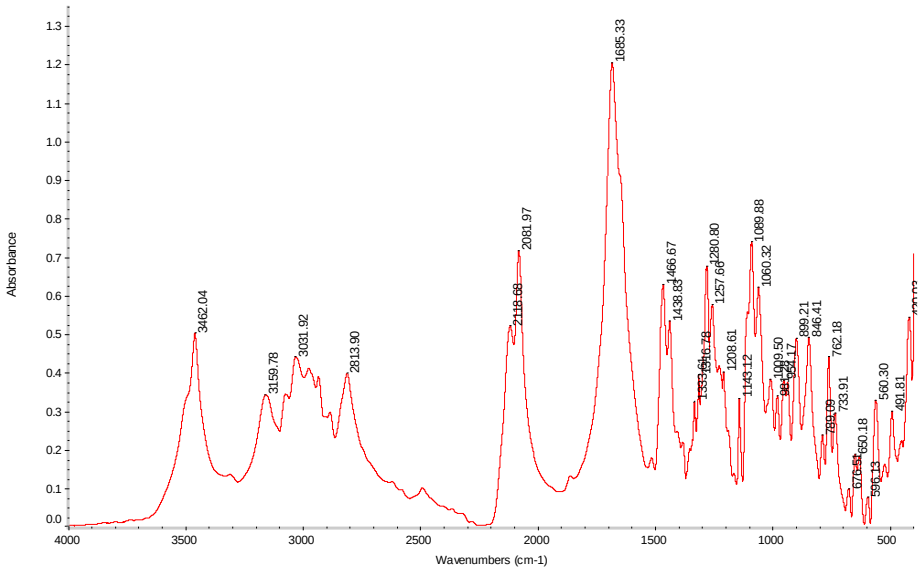
Drug release profile is evaluated in vitro using a dissolution test apparatus (TDT-06T, Electrolab, India). The USP Type II (paddle type) method was selected to perform the dissolution profile of Zidovudine. The dissolution for all the formulations was carried out according to US Pharmacopoeia [9] for 8 h in 0.1N HCl. The temperature was maintained at 37 ± 0.5°C and a constant paddle rotation speed of 50 rpm. Samples (10 ml) were withdrawn at afetr hours (regular intervals) and filtered through membrane filter (pore size 0.22 µm). The absorbance of diluted sample was measured spectrophotometrically at 270 nm using UV-visible (Shimadzu UV-Vis Spectrophotometer). Actual amount of released drug was determined from the calibration curve.

The optimized tablets of Zidovudine were kept in open Petri dishes and stored in a stability chamber maintained at 40 ± 2 °C and 75 ± 5 % RH (8).

Results and Discussion:

The FTIR spectra of Zidovudine and its blends were found to be identical. The principle FTIR absorption peaks of Zidovudine (Fig 2) at 3462.04 cm^{-1} (N-H Stretching), 3159.60 cm^{-1} (C-H Stretching), 2813.90 cm^{-1} (H-C=O: C-H stretching), 2081.97 cm^{-1} (C=C-H), 1685.33 cm^{-1} (C=O streching), 1200.69 cm^{-1} (C-N streching), 1099.18 cm^{-1} (C-O-C (Carbohydrate) and 762.53 cm^{-1} (CH_2 streching) were observed in Zidovudine as well as the formulations containing zidovudine. Thus the FTIR studies indicated that there were no drug-excipient interactions.

(A)



(B)

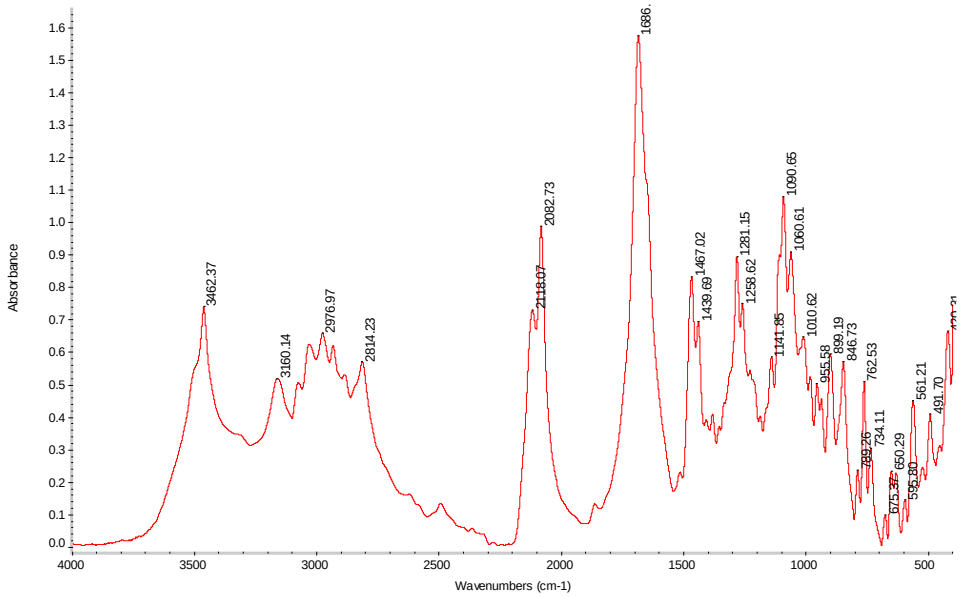
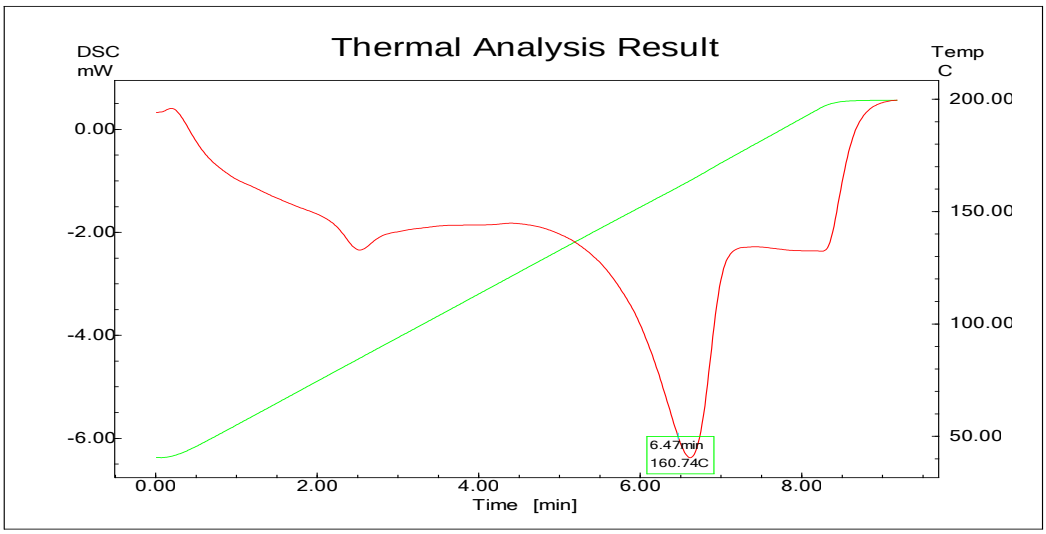


Fig. 1. Fourier transmission infra-red spectrum of A) Zidovudine alone B) Zidovudine with magnesium stearate.

The compatibility study between drug and excipients is carried out by DSC analysis. The study showed that no any interaction was found between drug and excipients in their physical mixture. The DSC study indicate the there were no Interaction between drug and excipients.

(A)



(B)

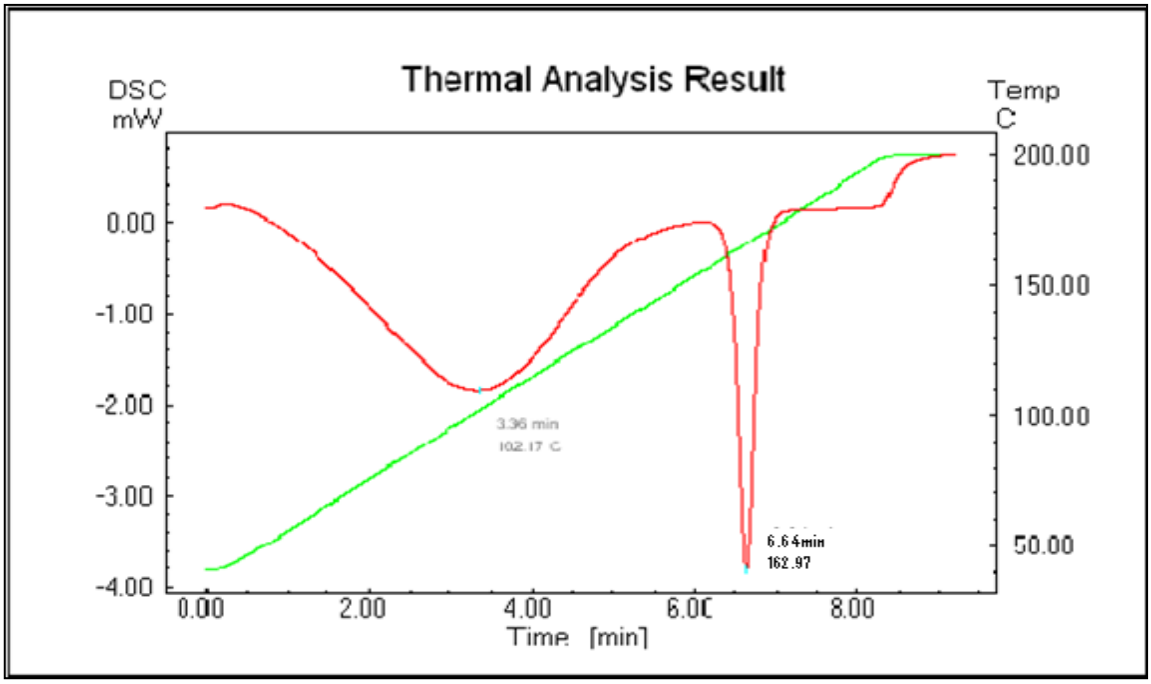


Figure 2: DSC thermogram of (A)Zidovudine and (B) Carbapol and othe excipients

The sustained release matrix tablet was prepared as per the formulation table no. 1 in formulation as direct compression vehicle and Carbopol and xanthan gum as controlled release polymer with at appropriate concentration. The tablets were evaluated after 3 months of storage under accelerated stability conditions (40 ± 2 °C and 75 ± 5 % RH), the results of which are presented in Table IV. It is evident that the formulation is stable in terms of drug concentration, disintegration time and time required to release.

Table 2. Evaluation of tablets after 1 months of storage at 40 °C and 75 % RH

Parameter	At 0 week	At 2 weeks	At 3weeks	At 4 weeks
Increase in weight	--	0.41±2.25	0.54±2.46	0.98±2.16
Hardness	5.0±0.25	4.5±0.36	4.0±0.46	4.0±0.52
Disintegration Time	40±2.52	30±2.63	30±2.41	25±2.47
in-vitro drug release	98.99±1.37	98.85±1.29	98.86±1.38	98.23±1.20

Conclusion:

The results obtain from the above studies confirmed that DSC and IR could be used as rapid methods to evaluate the compatibility between Zidovudine and excipients. In the present study highlighted the application of DSC and IR study for the rapid evaluation of the drug excipient compatibility. As the control and treatment of HIV infection is a challenge now a day, the anti-HIV drug such as Zidovudine was selected for current work. In this study successfully employed to assess the compatibility of zidovudine with the excipients used in the development of sustained release tablet formulations. There is no definite evidence of interaction was observed between zidovudine and the excipients used in the development of in-house formulations of sustained release tablets of Zidovudine.

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