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Research/Review

Formulation development and invitro characterization of dolutegravir sustained release matrix tablets

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Abstract

In our contemporary research work, constant effort has been put into deciding on herbal polymers such as Tragacanth, Acacia gum, and Thickener as obstructive polymers to allow design sustained launch capsules of Dolutegravir. All best subjected formulations limits had been fulfilled or passes the tests by means of the tablets after they had been set up, and their release kinetics effects are remarkable. Drug Excipient Compatibility studies revealed that there was no considerable change. FT-IR studies resulted that all peaks corresponding to different functional groups of pure drug were present in the drug-excipient mixtureno interaction between the dmg and excipients. To be specific the F2 formulations. Tragacanth, used to be proven to have the best drug delivery trait (99.19%) amongst all the formulations examined (12 hours). After the F2's more desirable formulation, used to be formulated.

Keywords: Dolutegravir, Tragacanth, Acaciagum, Thickener and Sustained release tablets.

INTRODUCTION

When in contrast to the three or extra instances each day that might also be required by means of separate and auxiliary traditional regimens to get a comparable robust effect, sustained launch capsules are typically taken solely as soon as or twice daily. Advantages consist of higher parent consistency and medical usability meant utility when a single dose is managed over a lengthy length of time to preserve a close to uniform or steady blood stage of a drug. Howard Press, located in New Jersey, furnished the crucial Sustained launch drugs in the 1950s. Developed the principal "Nitroglyn" pills underneath his related patent. Sustained release, deferred release, modified release, prolonged conveyance, and station programmes are all phrases used to describe drug distribution structures that are supposed to produce or increase therapeutic impact by using constantly conveying medicinal drug over a giant duration single piece. These labels are used to pick out the buildings in question.

The intention of the planning of supported or maintained transport structures is to both minimize there peat of the dose Oren large the medicine's practicality providing uniform sustained releases (SRs) like the grid pill

have superior the clever prescription motion shape in the pharmaceutical industry. Medicine launch charge from the estimating shape is regularly managed with the aid of the kind and extent of polymer used in the publications of action, and it prevents complicated manufacturing during collection. A SR estimation shape is usually fabricated the usage of a hydrophilic polymer system. The growing problem and price related with the improvement of novel prescription tablets hassled to a focal point on the improvement of supported transport mechanisms. System constructions are often employed, with the sole intention of facilitating delivery. The remedy that is diluted or disseminated is retrieved and its presence is managed via the motion structure.

MATERIALS AND METHODS

The materials used in this current research work are procured from reliable sources of dolutegravir, Livealth Biopharma, Tragacanth, LobaChemie Pvt. Ltd., Mumbai, India, Acaciagum, Merck Specialties Pvt. Ltd, Mumbai, India, Xanthangum, Aravind Remedies (AR), Chennai, India. All other reagents used I this research work are procured from most reliable vendors.

Determination of calibration curve

100mg of pure chug was dissolved in 10ml methanol (primarily stock solution - 1000µg/ml). From this primarily stock solution 10ml was pipette out into 100 ml volume tric flask and made it up to 10ml with the media (Secondary stock solution- 100tg/ml). From secondarily stock solution required concentrations were prepared and those concentrations absorbance were found out at required wave length.

Pre-formulation parameters

The quality of tablet, once formulated, is generally dictated by the quality of physicochemical properties of blends. There are many formulations and process va1iables involved in mixing and all these can affect the characteristics of blends produced. The various character listics of blends tested as per Indian Pharmacopoeia.

Formulation development of Tablets

All the formulations were compress by direct compression. The compositions of different formulations are given. The tablets were prepared as per the procedure given below and aim is to prolong the release of Dolutegravir. Total weight of the tablet was considered as 300mg.

Evaluation of postcompression parameters for prepared Tablets

The designed fo1mulation tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and dmg content.

Weight variation test

To study the weight variation, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight va1iation test would be a satisfacto1y method of dete1mining the drug content uniformity.

% Deviation = (Individual weight-Average weight /Average weight) x 100

Hardness

Hardness of a tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. For each formulation, the hardness of three tablets was determined using Monsanto hardness tester and the average is calculated and presented with deviation.

Thickness

Tablet thickness is an important characteristic in reproducing appearance. Tablet thickness is an important character isticinre producing appearance. Average thickness for core and coated tablets is calculated and presented with deviation.

Friability %

It is measured of mechanical strength of tablets. Roche friabilator was used to determine the friability by following procedure. Pre-weighed tablets were placed in friabilator. The tablets were rotated at 25rpm for 4 minutes (100 rotations). At the end of the test, the tablets are re-weighed, loss in the weight of tablet is the measure of friability and expressed in percentage as

%Friability = [(Wl-W2)/W] x 100

Determination of Drug Content

Tablets were tested for their drug content. Ten tablets were finely powdered and quantities of the powder equivalent to one tablet weight of drug were accurately weighed. The powder was then transferred to a 100ml volumetric flask containing 50ml of water and allowed to stand to ensure complete solubility of the drug. The mixture was made up to volume with media. The solution was suitably diluted and the absorption was determined by UV-Visible spectrophotometer. The drug concentration was calculated from the calibration curve.

***Invitro* drug release studies**

The 900 ml of 0.1M HCl was placed in a vessel and the USP apparatus-II (Paddle Method) was assembled. The medium was allowed to equilibrate to a temperature of 37°C ± 0.5°C. The tablet was placed in the vessel and the apparatus was operated for 2 hours. Then the 0.1M HCl was removed and pH 6.8 phosphate buffer was added. The process was continued for up to 12 hours at 50 rpm. At definite time intervals, 5 ml of sample was withdrawn, filtered, and then 5 ml of media was replaced. Suitable dilutions were done with media and analyzed spectro-photometrically at the required wavelength using a UV-spectrophotometer at 262 nm.

Application of release rate kinetics to dissolution data

Various models were tested for explaining the kinetics of chug release. To analyze themechaJ1ism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

Zero order release rate kinetics

To study the zero – order release kinetics the release rate data are fitted to the following equation.

F =Ko t

First order release rate kinetics

The release rate data are fitted to the following equation **Log (100-F)=kt**

Higuchi release model

To study the Higuchi release kinetics, the release rate data were fitted to the following equation. **F =ktl/2**

Korsmeyer and Peppas release model

The mechanism of drug release was evaluated by plotting the log percentage of ch11g released versus log time according to Korsmeyer – Peppas equation. The exponent 'n' indicates the mechanism of drug release calculated through the slope of the straight Line.

$$Mt/Mee = K\,t^{0}$$

Hixson-Crowell release model: $(100-Qt)^{113} = 100^{113} - Kn{:}c.t$

Drug-excipient compatibility studies

Fouriertrans form infrared (FTIR) spectroscopy

The compatibility between the pure chug and excipients was detected by FTIR spectra obtained on Bernker FTIR Germany(Alpha T).The solid powder sample directly place on yellow c1ystal which was made up of ZnSe. TI1e spectra were recorded over the wave number of 4000 cm^{-1} to 400cm^{-1}.

RESULTS & DISCUSSION

The present study was aimed to developing sustained release tablets of Dolutegravir using various polymers. All the fo1mulations were evaluated for physicochemical properties and *in vitro* drug release study.

Analytical method

Graphs of Dolutegravir were taken in 0.l N HCL and in pH 6.8 phosphate buffer at 259 nm and 263 nm respectively as shown in the figure 1&2.

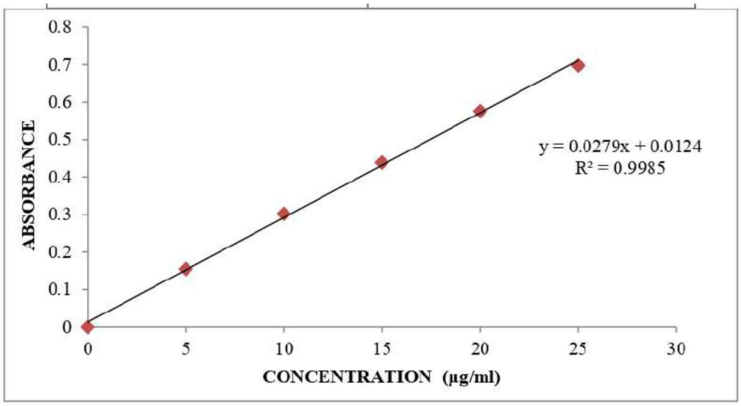

Fig 1: Standard curve of Dolutegravir

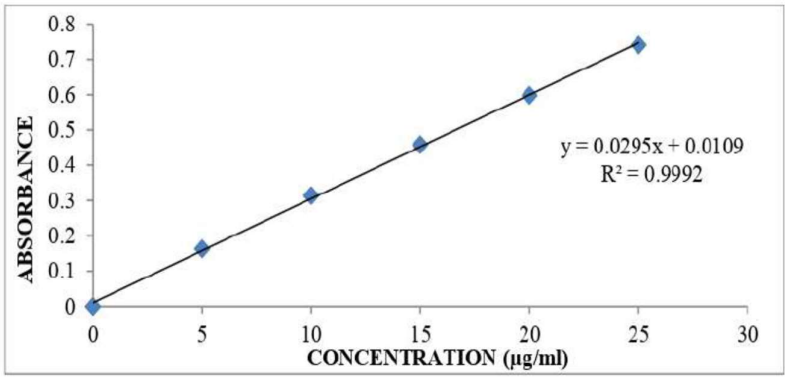

Fig 2: Standard curve of Dolutegravir

Quality control parameters for tablets

Tablet quality control tests such as weight variation, hardness, friability, thickness, and drug release studies in different media werepe1fonnedon the compression tablet.

Weight variation test

Tablets of each batch were subjected to weight variation test, difference in weight and percent deviation was calculated for each tablet. The average weight of the tablet is approximately in range of 296.50 to300.05mg, so the pe1missiblelimitis ±7.5% (>300 mg). The results of the test showed that, the tablet weights were within the limit.

***In-vitro* Drug Release Studies**

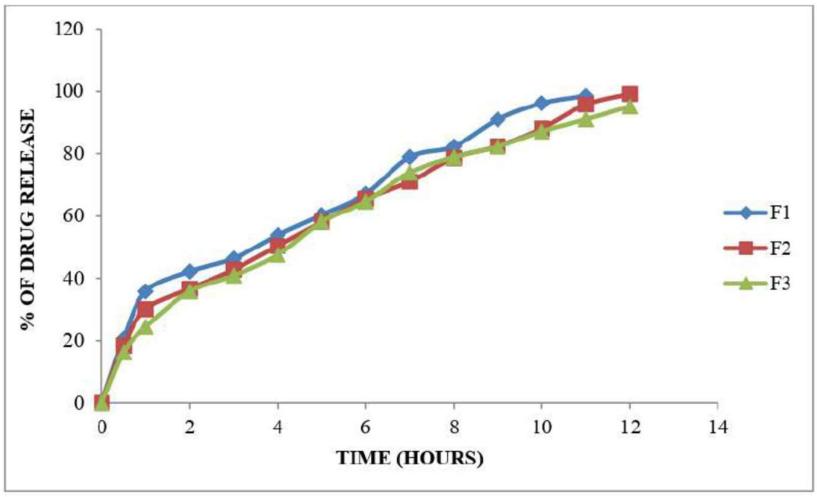

Fig 3: Dissolution profile of Dolutegravir (Fl, F2 and F3 formulations)

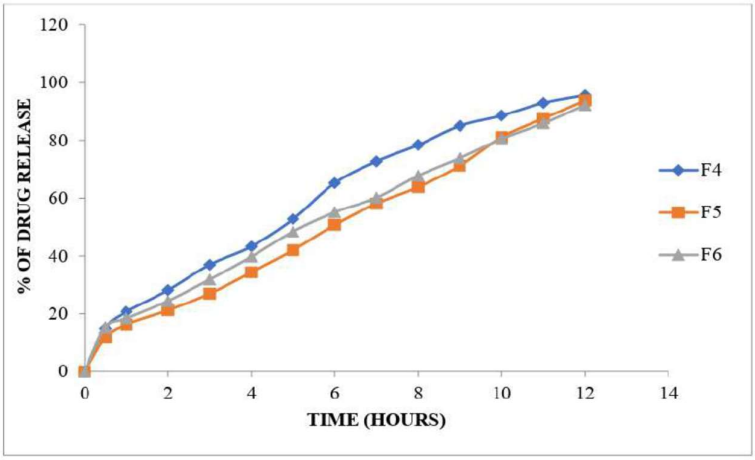

Fig 4: Dissolution profile of Dolutegravir (F4, FS and F6 formulations)

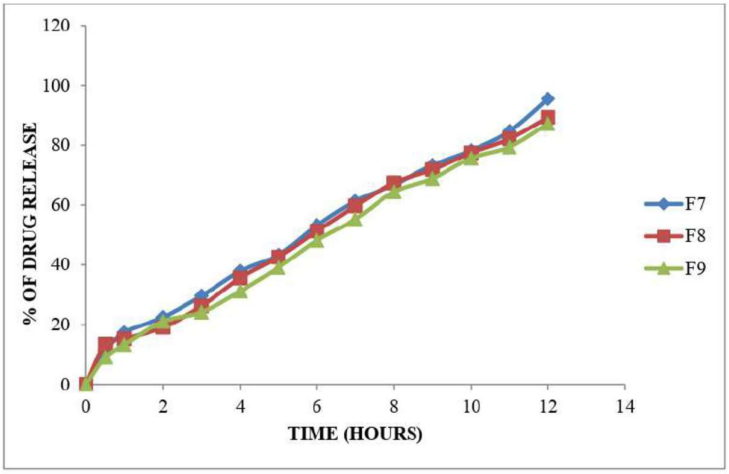

Fig 5: Dissolution profile of Dolutegravir (F7, F8 and F9 formulations)

Different formulation (Fl-F9)were prepared using different polymers like Tragacanth, Acacia gum and Xanthan gum alone at different ratios. formulationFl-I3 were prepared using Tragacanth at the ratio of 1:1, 1:2 and 1:3 which showed the drug release about 98.56% at 11h, 99.19% at 12hand 95.14at 12h %. Formulations F4-F6 were prepared using Acacia gum at the ratio of I:1,1:2 and **1**:3 with the drug releaseof95.63%, 93.75and92.16 %and the formulations F7-F9 were prepared by using Xanthan gumpolymerattheratioof1:1,1:2and1:3Showedthedrugrelease of95.49%,89.28% and 87.19 % at the end of 12 h. Among all these fo1mulations F2 was selected as the best ideal formulation which exhibited 99.19 % of drug release in 12 h as shown in the figures 3, 4&5.Finally, it can be Concluded that F2 formulation was considered as optimized formulation.

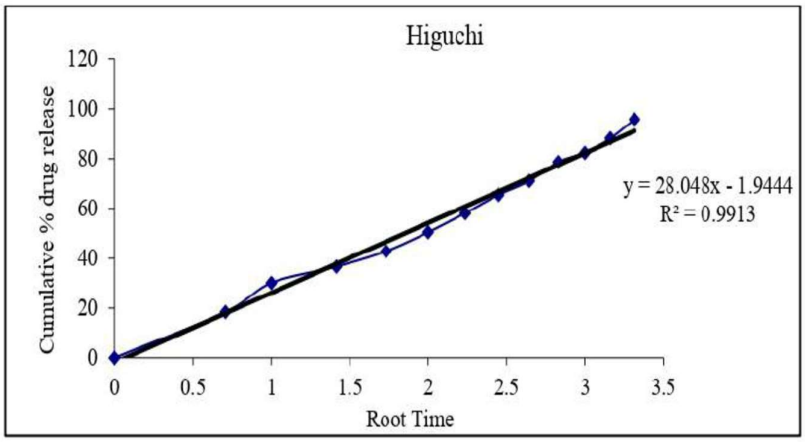

Fig 6: Higuchi release kinetics graph

From the above graphs it was evident that the formulationF2 was followed Higuchi release kinetics mechanism as shown in the figure 6.

Drug-Excipient compatibility studies

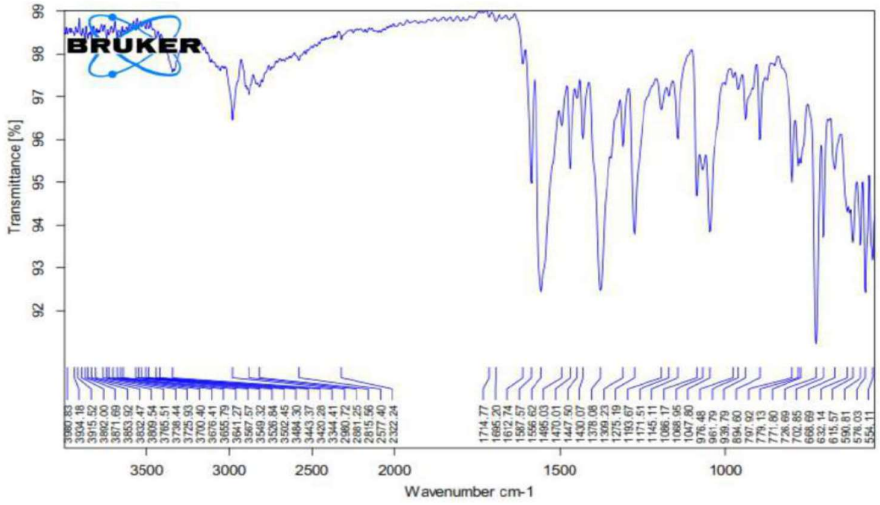

Fig 7: FT-TR Spectrum of Dolutegravir pure drug

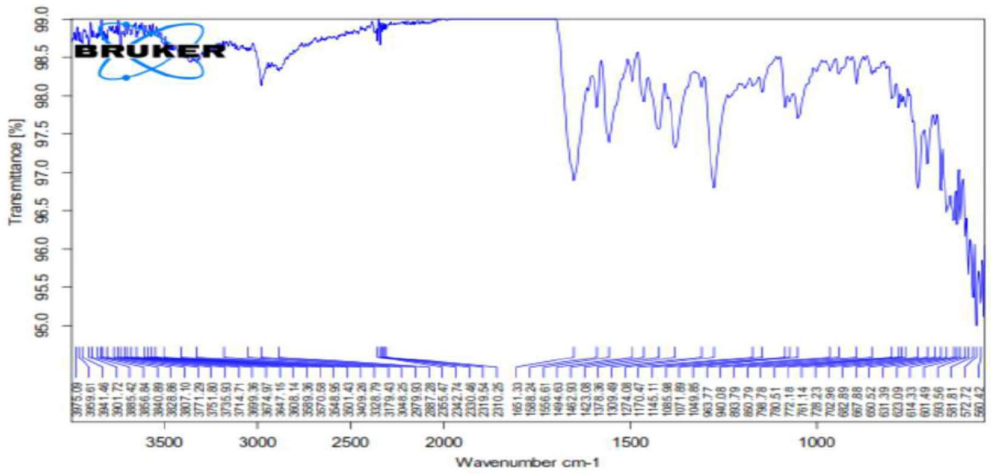

Fig 8: FTIR Spectrum of Optimized Formulation

From the above studies it was found that there was no shifting in the major peaks which indicated that there were no significant interactions occurred between the Dolutegravir and excipients used in the preparation of different Dolutegravir Sustained release formulations. TI1erefore the dmg and excipients are compatible to form stable.

Formulations under study, The FTIR spectra of Dolutegravir and physical mixture used for optimizedfo1mulationwere obtained and these are depicted in above figures 7&8.From the FTIR data it was evident that t11e dmg and excipients does not have any interactions. Hence they were compatible.

CONCLUSION

In this context, our present study was carried out to evaluate the natural polymers for its matrix forming ability due to formation of thick gel structures, so we concluded that Tragacanth, Acacia Gumand, and Xanthan gum-formulated tablets were found to be effective in sustaining the drug release up to 12 hrs. During this study, it was also found that polymer concentration influences the dmg release behavior. Drug Excipient Compatibility Studies revealed that there was no considerable change. FTIR studies resulted in all peaks corresponding to different functional groups of pure drug were present in the drug-excipient mixture with no interaction between the dmg and excipients. It can be concluded that a stable formulation could be developed by incorporating Tragacanth polymer in a definite proportion, so that the sustained released profile is maintained for a sustained release. Release model of sample was found to follow Higuchi release kinetics mechanism with high linearity.

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