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# FORMULATION AND IN-VITRO EVALUATION OF DALFAMPRIDINE SUSTAINED RELEASE TABLETS USING VARIOUS POLYMERS

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**Abstract:**

*In present investigation the sustained release tablets of Dalfampridine was formulated to study effect of various natural polymers using Tragacanth, Acacia gum and Xanthan gum. The model is based on a novel dosage form designed to deliver a drug into the gastrointestinal tract in a controlled manner. Matrix tablets were prepared by direct compression method. As a pre- requisite and part of pre-formulation studies, drug along with selected excipients and as optimized formulation was subjected to FT-IR studies. It was found that no interaction among excipients occurred, as no extra peaks obtained. Tablets were evaluated for various IPQC tests like hardness, friability, content uniformity and in-vitro drug release by USP paddle apparatus. It was found that the release of drug D3 formulation showed 99.83% the formulation gave better release amongst formulations, showing highest release following Peppas release kinetics.*

***Key words:*** *Dalfampridine, Tragacanth, Acacia gum, Xanthan gum, direct compression and Sustained release matrix tablets.*

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## INTRODUCTION:

Sustained release tablets are commonly taken only once or twice daily, compared with counterpart conventional forms that may have to take three or four times daily to achieve the same therapeutic effect [1-3]. The advantage of administering a single dose of a drug that is released over an extended period of time to maintain a near-constant or uniform blood level of a drug often translates into better patient compliance, as well as enhanced clinical efficacy of the drug for its intended use [4-6]. The mechanistic analysis of controlled release of drug reveals that partition coefficient; diffusivity; diffusional path thickness and other system parameters play various rate determining roles in the controlled release of drugs from either capsules, matrix or sandwich type drug delivery systems [7-12].

**A) Polymer hydration:**

It is important to study polymer hydration/swelling process for the maximum number of polymers and polymeric combinations. The more important step in polymer dissolution include absorption/adsorption of water in more accessible places, rupture of polymer-polymer linking with the simultaneous forming of water-polymer linking, separation of polymeric chains, swelling and finally dispersion of polymeric chain in dissolution medium [13-15].

**B) Drug solubility:**

Molecular size and water solubility of drug are important determinants in the release of drug from swelling and erosion controlled polymeric matrices. For drugs with reasonable aqueous solubility, release of drugs occurs by dissolution in infiltrating medium and for drugs with poor solubility release occurs by both dissolution of drug and dissolution of drug particles through erosion of the matrix tablet [16-18].

**C) Solution solubility:**

In view of in vivo (biological) sink condition maintained actively by hem perfusion, it is logical that all the in vitro drug release studies should also be conducted under perfect sink condition. In this way a better simulation and correlation of in vitro drug release profile with in vivo drug administration can be achieved. It is necessary to maintain a sink condition so that the release of drug is controlled solely by the delivery system and is not affected or complicated by solubility factor [19-22].

**D) Polymer diffusivity:**

The diffusion of small molecules in polymer structure is energy activated process in which the diffusant molecules moves to a successive series of equilibrium position when a sufficient amount of energy of activation for diffusion Ed has been acquired by the diffusant is dependent on length of polymer chain segment, cross linking and crystallinity of polymer.

The release of drug may be attributed to the three factors viz,

i. Polymer particle size

ii. Polymer viscosity

iii. Polymer concentration.

**i. Polymer particle size:** Malamataris stated that when the content of hydroxyl propyl methylcellulose is higher, the effect of particle size is less important on the release rate of propranolol hydrochloride, the effect of this variable more important when the content of polymer is low. He also justified these results by considering that in certain areas of matrix containing low levels of hydroxyl propyl methylcellulose led to the burst release.

**ii. Polymer viscosity:**

With cellulose ether polymers, viscosity is used as an indication of matrix weight. Increasing the molecular weight or viscosity of the polymer in the matrix formulation increases the gel layer viscosity and thus slows drug dissolution. Also, the greater viscosity of the gel, the more resistant the gel is to dilution and erosion, thus controlling the drug dissolution.

**iii. Polymer concentration:**

An increase in polymer concentration causes an increase in the viscosity of gel as well as formulation of gel layer with a longer diffusional path. This could cause a decrease in the effective diffusion coefficient of the drug and therefore reduction in drug release. The mechanism of drug release from matrix also changes from erosion to diffusion as the polymer concentration increases.

The goal in designing sustained or sustained delivery systems is to reduce the frequency of the dosing or to increase effectiveness of the drug by localization at the site of action, reducing the dose required or providing uniform drug delivery. So, sustained release dosage form is a dosage form that release one or more drugs continuously in predetermined pattern for a fixed period of time, either systemically or to a specified target organ [7-11].

## MATERIALS AND METHODS:

**Materials:** dalfampridine was purchased from Raxuter chemicals, surat, Gujarat. Aerosol purchased from Alkem laboratories Mumbai, Maharashtra. Sigma Aldrich, Mumbai. Magnesium stearate purchased from Triveni chemicals, Mumbai. polyvinyl pyrrolidone K30, Xanthan Gum, Tragacanth Gum, Acacia Gum purchased from Kapadia Gumchem industries Mumbai, Maharashtra.

**Methods:**

**Determination of λ max:** 100mg of pure drug was dissolved in 10ml methanol (primary stock solution - 1000 µg/ml). From this primary stock solution 1 ml was pipette out into 100 ml volumetric flask and made it up to 100ml with the media (Secondary stock solution–100µg/ml). From secondary stock solution again 1ml was taken it in to another volumetric flask and made it up to 10 ml with media (working solution - 10µg/ml). The working solution was taken for determining the wavelength.

**Determination of calibration curve:**100mg of pure drug was dissolved in 10ml methanol (primary stock solution - 1000 µg/ml). From this primary stock solution 10 ml was pipette out into 100 ml volumetric flask and made it up to 10ml with the media (Secondary stock solution – 100µg/ml). From secondary stock solution required concentrations were prepared (shown in Table 8.1 and 8.2) and those concentrations absorbance were found out at required wavelength.

**Pre-formulation parameters:** The quality of tablet, once formulated by rule, is generally dictated by the quality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all these can affect the characteristics of blends produced. The various characteristics of blends tested as per Indian Pharmacopoeia.

**Angle of repose:** The frictional force in a loose powder can be measured by the angle of repose. It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides of the pile until the mutual friction of the particles producing a surface angle, is in equilibrium with the gravitational force. The fixed funnel method was employed to measure the angle of repose. A funnel was secured with its tip at a given height (h), above a graph paper that is placed on a flat horizontal surface. The blend was carefully pored through the funnel until the apex of the conical pile just touches the tip of the funnel. The radius (r) of the base of the conical pile was measured. The angle of repose was calculated using the following formula:

$\tan \theta = h / r$
$\tan \theta$ = Angle of repose
h = Height of the cone,
r = Radius of the cone base

**Bulk density:** Density is defined as weight per unit volume. Bulk density, is defined as the mass of the powder divided by the bulk volume and is expressed as gm/cm3. The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together. Bulk density is very important in the size of containers needed for handling, shipping, and storage of raw material and blend. It is also important in size blending equipment. 10 gm powder blend was sieved and introduced into a dry 20 ml cylinder, without compacting. The powder was carefully leveled without compacting and the unsettled apparent volume, Vo, was read.
The bulk density was calculated using the formula:

Bulk Density = M / Vo

Where, M = weight of sample

Vo = apparent volume of powder

**Tapped density:** After carrying out the procedure as given in the measurement of bulk density the cylinder containing the sample was tapped using a suitable mechanical tapped density tester that provides 100 drops per minute and this was repeated until difference between succeeding measurement is less than 2 % and then tapped volume, V measured, to the nearest graduated unit. The tapped density was calculated, in gm per L, using the formula:

Tap = M / V Where, Tap= Tapped Density

M = Weight of sample

V= Tapped volume of powder

**Measures of powder compressibility:** The Compressibility Index (Carr's Index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities. In theory, the less compressible a material the more flowable it is. As such, it is measures of the relative importance of interparticulate interactions. In a free-flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value.

For poorer flowing materials, there are frequently greater interparticle interactions, and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the Compressibility Index which is calculated using the following formulas:

Carr's Index = [(tap - b) / tap] × 100 Where, b = Bulk Density
Tap = Tapped Density

**Formulation development of Tablets:** All the formulations were compress by direct compression. The compositions of different formulations are given in Table 7.4. The tablets were prepared as per

the procedure given below and aim is to prolong the release of Dalfampridine. Total weight of the tablet was considered as 120mg.

**Procedure:**

1)Dalfampridine and all other ingredients were individually passed through sieve no ≠ 60.

2)All the ingredients were mixed thoroughly by triturating up to 15 min.

3)The powder mixture was lubricated with talc.

4)The tablets were prepared by using direct compression method.

**Table 1: Formulation composition for tablets**

| INGREDIENTS (MG) | FORMULATION | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | D1 | D2 | D3 | D4 | D5 | D6 | D7 | D8 | D9 |
| Dalfampridine | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| Tragacanth | 10 | 20 | 30 | - | - | - | - | - | - |
| Acacia gum | - | - | - | 10 | 20 | 30 | - | - | - |
| Xanthan gum | - | - | - | - | - | - | 10 | 20 | 30 |
| PVP-K 30 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| Aerosil | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Magnesium Stearate | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| MCC | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s |
| Total Weight | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 |

**Drug–excipient compatibility studies**

**Fourier transform infrared (FTIR) spectroscopy:** The compatibility between the pure drug and excipients was detected by FTIR spectra obtained on Bruker FTIR Germany (Alpha T). The solid powder sample directly place on yellow crystal which was made up of ZnSe. The spectra were recorded over the wave number of 4000 cm-1 to 400 cm-1.

**Evaluation of post compression parameters for prepared Tablets**

The designed formulation tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug 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 variation test would be a satisfactory method of determining the drug content uniformity. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in the following table and none deviate by more than twice the percentage. The mean and deviation were determined. The percent deviation was calculated using the following formula.

% Deviation = (Individual weight – Average weight / Average weight) × 100

**Table 2: Pharmacopoeial specifications for tablet weight variation**

| Average weight of tablet (mg) (I.P) | Average weight of tablet (mg) (U.S.P) | Maximum percentage difference allowed |
|---|---|---|
| Less than 80 | Less than 130 | 10 |
| 80-250 | 130-324 | 7.5 |
| More than 250 or More | More than 324 | 5 |

**Hardness:** Hardness of 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 characteristic in reproducing 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 the friabilator. The tablets were rotated at 25 rpm for 4 minutes (100 rotations). At the end of test, the tablets were re weighed, loss in the weight of tablet is the measure of friability and is expressed in percentage as
% Friability = [( W1-W2) / W] × 100 Where, W1 = Initial weight of three tablets
W2 = Weight of the three tablets after testing

**Determination of drug content:** Tablets were tested for their drug content. Ten tablets were finely powdered quantities of the powder equivalent to one tablet weight of drug were accurately weighed, transferred to a 100 ml volumetric flask containing 50 ml water and were 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-dissolution studies:** 900ml 0f 0.1 HCl was placed in vessel and the USP apparatus–II (Paddle Method) was assembled. The medium was allowed to equilibrate to temp of 37°c + 0.5°c. Tablet was placed in the vessel and apparatus was operated for 2 hours and then the media 0.1 N HCl were removed and pH 6.8 phosphate buffer was added process was continued up to 12 hrs at 50 rpm. At definite time intervals withdrawn 5 ml of sample, filtered and again 5ml media was replaced. Suitable dilutions were done with media and analyzed by spectrophotometrically at required wavelength using UV-spectrophotometer at 262.

**Application of release rate kinetics to dissolution data:** Various models were tested for explaining the kinetics of drug release. To analyze the mechanism 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 ar e fitted to the following equation.
F = Ko t
Where, 'F' is the drug release at time't', and 'Ko' is the zero order release rate constant. The plot of % drug release versus time is linear.

**First order release rate kinetics:** The release rate data are fitted to the following equation
Log (100-F) = kt
A plot of log cumulative percent of drug remaining to be released vs. time is plotted then it gives first order release.

**Higuchi release model:** To study the Higuchi release kinetics, the release rate data were fitted to the following equation.
F = k t1/2
Where, 'k' is the Higuchi constant.
In higuchi model, a plot of % drug release versus square root of time is linear.

**Korsmeyer and Peppas release model:** The mechanism of drug release was evaluated by plotting the log percentage of drug 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/ M∞ = K tn
Where, Mt/ M∞ is fraction of drug released at time 't', k represents a constant, and 'n' is the diffusional exponent, which characterizes the type of release mechanism during the dissolution process. For non-Fickian release, the value of n falls between 0.5 and 1.0; while in case of Fickian diffusion, n = 0.5; for zero-order release (case I I transport), n=1; and for supercase II transport, n> 1. In this model, a plot of log (Mt/ M∞) versus log (time) is linear.

**Hixson-Crowell release model:** Hixson-Crowell model describes the release of drugs from an insoluble matrix through mainly erosion. (Where there is a change in surface area and diameter of particles or tablets).
(100-Qt)1/3 = 1001/3– KHC.t
Where, k is the Hixson-Crowell rate constant.

**Results and discussion:**
The present study was aimed to developing sustained release tablets of Dalfampridine using various polymers. All the formulations were evaluated for physicochemical properties and *in vitro* drug release study.

**Analytical method**
Graphs of Dalfampridine were taken in 0.1N HCL and in pH 6.8 phosphate buffer at 247 nm and 250 nm respectively.

**Table 3: Observations for graph of Dalfampridine in 0.1N HCL**

| Concentration (µg/ml) | Absorbance |
|---|---|
| 0 | 0 |
| 10 | 0.138 |
| 20 | 0.266 |
| 30 | 0.397 |
| 40 | 0.511 |
| 50 | 0.635 |

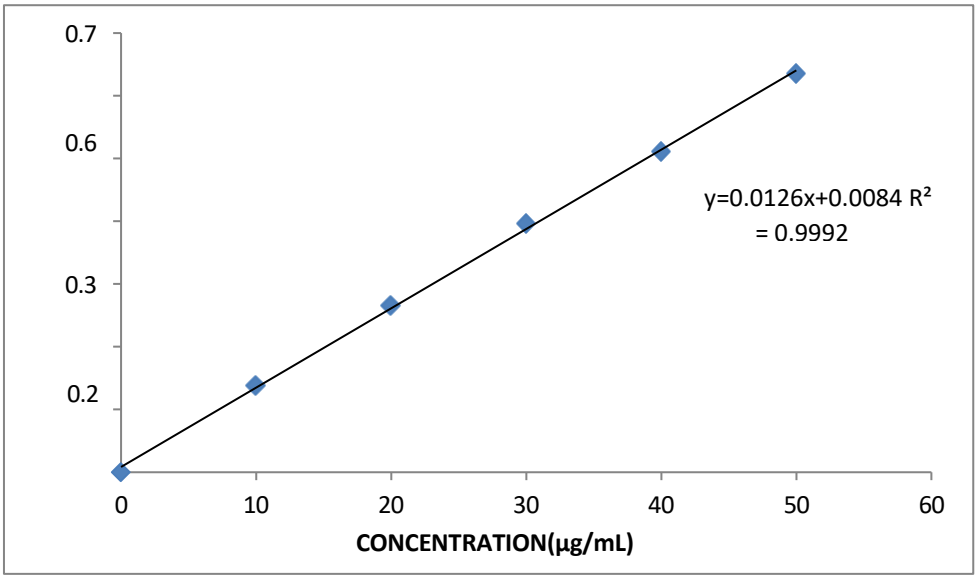


**Figure 1: Standard curve of Dalfampridine**

**Pre-formulation parameters of powder blend**

**Table 4: Pre-formulation parameters of Core blend**

| Formulation Code | Angle of Repose | Bulk density (gm/ml) | Tapped density (gm/ml) | Carr's index (%) | Hausner's Ratio |
|---|---|---|---|---|---|
| D1 | 24.72 ± 0.01 | 0.345 ± 0.018 | 0.401 ± 0.012 | 13.97 ± 0.01 | 1.16 ± 0.02 |
| D2 | 19.66 ± 0.02 | 0.332 ± 0.002 | 0.375 ± 0.015 | 11.46 ± 0.01 | 1.13 ± 0.01 |
| D3 | 20.16 ± 0.015 | 0.465 ± 0.015 | 0.532 ± 0.001 | 12.59 ± 0.01 | 1.14 ± 0.01 |
| D4 | 21.41 ± 0.01 | 0.421 ± 0.002 | 0.492 ± 0.002 | 14.43 ± 0.02 | 1.17 ± 0.02 |
| D5 | 20.60 ± 0.015 | 0.382 ± 0.001 | 0.439 ± 0.002 | 12.98 ± 0.01 | 1.15 ± 0.01 |
| D6 | 20.36 ± 0.015 | 0.523 ± 0.002 | 0.604 ± 0.017 | 13.41 ± 0.02 | 1.15 ± 0.01 |
| D7 | 19.98 ± 0.01 | 0.348 ±0.001 | 0.401 ± 0.001 | 13.22 ± 0.01 | 1.15 ± 0.01 |
| D8 | 40.13 ± 0.01 | 0.412 ±0.015 | 0.530 ±0.021 | 22.23 ± 0.01 | 1.29 ± 0.01 |
| D9 | 39.90 ± 0.01 | 0.424 ± 0.001 | 0.517 ± 0.01 | 18.00 ± 0.01 | 1.21 ± 0.01 |

All the values represent n=3

Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range showing that the powder has good flow properties. The tapped density of all the formulations powders has good flow properties. The compressibility index of all the formulations was found to be 11.46 to 22.23 which show that the powder has good flow properties. All the formulations has shown the hausner ratio 1.13 to 1.29 indicating the powder has good flow properties.

**Quality control parameters for tablets:** Tablet quality control tests such as weight variation, hardness, friability, thickness, and drug release studies in different media were performed on the compression tablet.

**Table 5: Quality control parameters for tablets**

| Formulation codes | Weight variation (mg) | Hardness ($kg/cm^2$) | Friability (% loss) | Thickness (mm) | Drug content (%) |
|---|---|---|---|---|---|
| D1 | 119.69 | 5.8 | 0.58 | 3.18 | 96.52 |
| D2 | 120.04 | 5.1 | 0.34 | 3.99 | 99.60 |
| D3 | 118.76 | 5.7 | 0.25 | 3.82 | 98.14 |
| D4 | 116.25 | 5.0 | 0.49 | 3.71 | 97.50 |
| D5 | 119.03 | 5.4 | 0.66 | 3.90 | 99.13 |
| D6 | 117.42 | 5.9 | 0.72 | 3.65 | 98.36 |
| D7 | 119.78 | 5.6 | 0.31 | 3.59 | 96.42 |
| D8 | 118.45 | 5.4 | 0.26 | 3.98 | 99.14 |
| D9 | 118.14 | 5.2 | 0.44 | 3.85 | 98.73 |

**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 116.25 to 120.04 mg, so the permissible limit is ±7.5% (>120 mg). The results of the test showed that, the tablet weights were within the limit.

**Hardness test:** Hardness of the five tablets of each batch was checked by using Pfizer hardness tester and the data's were shown in Table 4. The results showed that the hardness of the tablets is in range of 5.0 to 5.9 kg/cm2, which was within IP limits.

**Thickness:** Thickness of five tablets of each batch was checked by using Micrometer and data shown in Table 4. The result showed that thickness of the tablet is raging from 3.18 to 3.99 mm.

Friability:

Tablets of each batch were evaluated for percentage friability and the data were shown in the Table 4. The average friability of all the formulations was less than 1% as per official requirement of IP indicating a good mechanical resistance of tablets.

**Drug content:** Drug content studies were performed for the prepared formulations. From the drug content studies, it was concluded that all the formulations were showing the % drug content values within 96.42 - 99.60 %. All the parameters such as weight variation, friability, hardness, thickness and drug content were found to be within limits.

***IN VITRO* DRUG RELEASE STUDIES**

**Table 6: Dissolution data of Dalfampridine tablets D1-D9**

| Time (H) | % OF DRUG RELEASE | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | D1 | D2 | D3 | D4 | D5 | D6 | D7 | D8 | D9 |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0.5 | 16.93 | 21.60 | 10.49 | 19.36 | 15.82 | 12.93 | 06.19 | 10.28 | 12.39 |
| 1 | 28.56 | 27.08 | 16.16 | 27.83 | 22.91 | 18.58 | 10.82 | 15.34 | 19.55 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 2 | 39.71 | 33.14 | 25.58 | 33.91 | 28.37 | 23.32 | 18.75 | 20.64 | 25.02 |
| 3 | 45.82 | 40.95 | 32.14 | 40.76 | 34.59 | 28.96 | 23.90 | 26.12 | 30.34 |
| 4 | 56.63 | 46.39 | 40.99 | 45.29 | 41.76 | 31.84 | 29.16 | 33.86 | 37.19 |
| 5 | 62.50 | 52.14 | 48.75 | 52.78 | 47.23 | 36.12 | 35.35 | 42.92 | 42.88 |
| 6 | 66.97 | 60.82 | 55.68 | 57.12 | 55.99 | 42.59 | 40.71 | 46.14 | 50.92 |
| 7 | 78.65 | 65.79 | 62.83 | 66.89 | 61.87 | 48.76 | 46.45 | 53.08 | 56.17 |
| 8 | 84.96 | 73.62 | 67.94 | 70.34 | 67.50 | 54.88 | 53.59 | 60.36 | 64.93 |
| 9 | 96.53 | 80.26 | 73.58 | 79.29 | 72.14 | 58.09 | 61.73 | 67.76 | 71.87 |
| 10 | | 92.81 | 81.06 | 84.86 | 76.99 | 63.23 | 78.96 | 75.33 | 77.15 |
| 11 | | 97.36 | 92.23 | 87.53 | 81.12 | 69.24 | 81.11 | 87.98 | 85.99 |
| 12 | | | 99.83 | 93.14 | 87.39 | 75.16 | 88.95 | 91.46 | 95.38 |

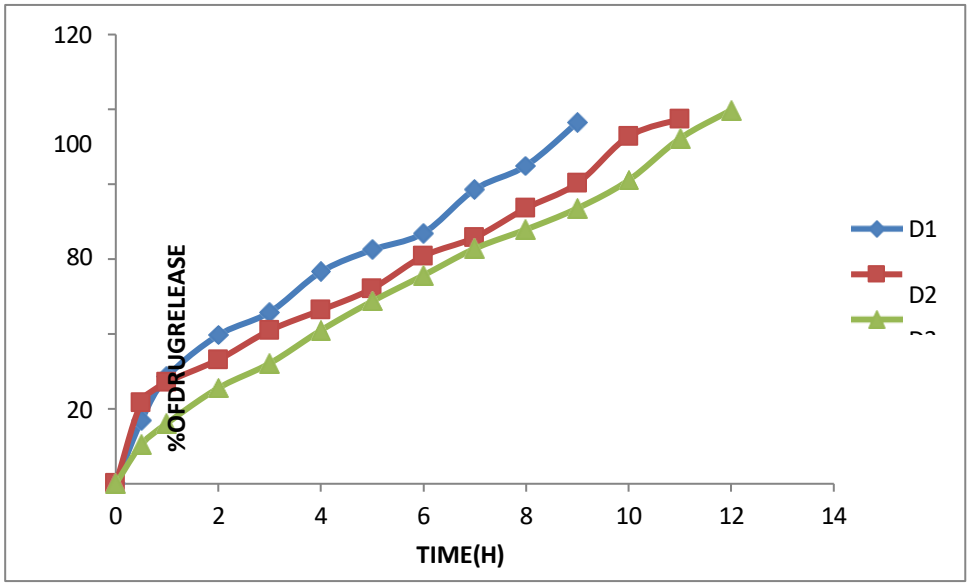


**Figure 2: Dissolution profile of Dalfampridine (D1, D2 and D3 formulations)**

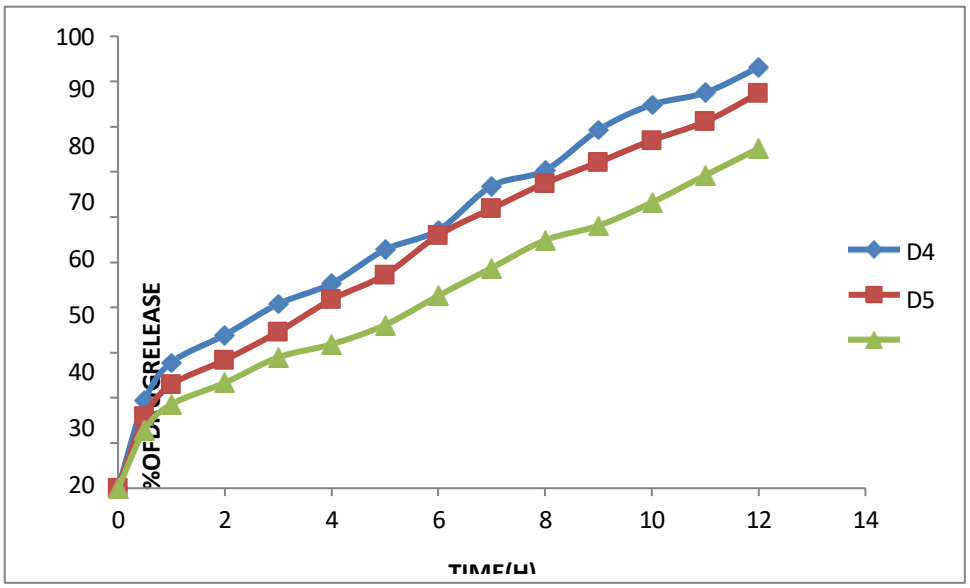


**Figure 3: Dissolution profile of Dalfampridine (D4, D5 and D6 formulations)**

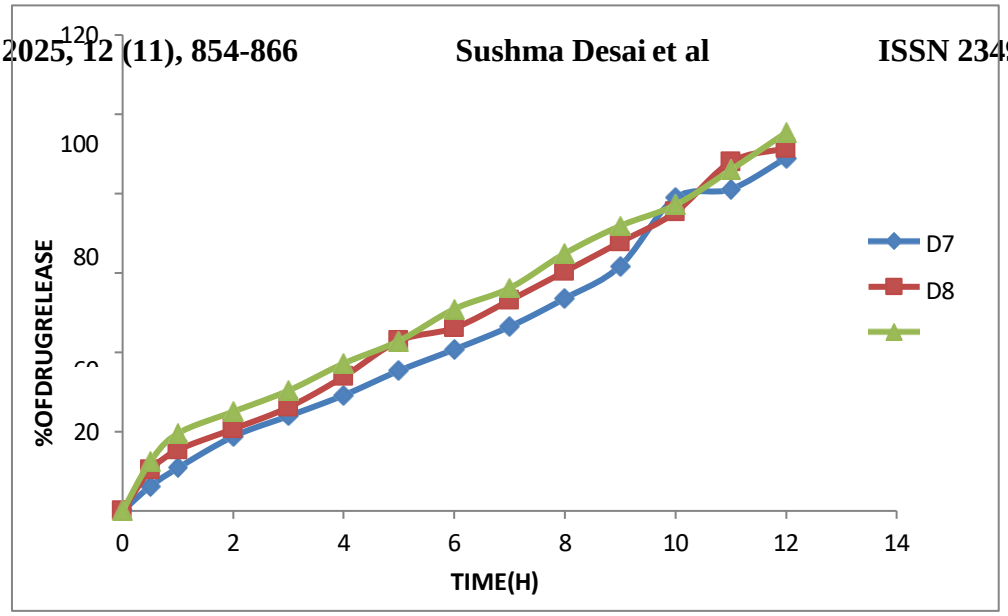


**Figure 4: Dissolution profile of Dalfampridine (D7, D8 and D9 formulations)**

Different formulations (D1-D9) were prepared using different polymers like Tragacanth, Acacia gum and Xanthan gum alone at different ratios. Formulations D1-D3 were prepared using Tragacanth at the ratio of 1:1, 1:2 and 1:3 which showed the drug release about 96.53% at 9h, 97.36% 11h and 99.83 at 12h %.
Formulations D4-D6 were prepared using Acacia gum at the ratio of 1:1, 1:2 and 1:3 with the drug release of 93.14%, 87.39 and 75.16% and the formulations D7-D9 were prepared by using Xanthan gum polymer at the ratio of 1:1, 1:2 and 1:3 Showed the drug release of 88.95%, 91.46% and 95.38% at the end of 12 h. Among all these formulations D3 was selected as the best ideal formulation which exhibited 99.83% of drug release in 12 h. Finally Concluded that D3 formulation was considered as optimized formulation.

**Table 7: Release kinetics:**

| CUMULATIVE (%) RELEASE Q | TIME (T) | ROOT (T) | LOG(%) RELEASE | LOG (T) | LOG (%) REMAIN | RELEASE RATE (CUMULATIVE % RELEASE / t) | 1/CUM % RELEASE | PEPPAS log Q/100 | % Drug Remaining | Q0 1/3 | Qt 1/3 | Q0 1/3 - Qt 1/3 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 0 | 0 | 0 | | | 2.000 | | | | 100 | 4.642 | 4.642 | 0.000 |
| 10.49 | 0.5 | 0.707 | 1.021 | -0.301 | 1.952 | 20.980 | 0.0953 | -0.979 | 89.51 | 4.642 | 4.473 | 0.168 |
| 16.16 | 1 | 1.000 | 1.208 | 0.000 | 1.923 | 16.160 | 0.0619 | -0.792 | 83.84 | 4.642 | 4.377 | 0.265 |
| 25.58 | 2 | 1.414 | 1.408 | 0.301 | 1.872 | 12.790 | 0.0391 | -0.592 | 74.42 | 4.642 | 4.206 | 0.435 |
| 32.14 | 3 | 1.732 | 1.507 | 0.477 | 1.832 | 10.713 | 0.0311 | -0.493 | 67.86 | 4.642 | 4.079 | 0.563 |
| 40.99 | 4 | 2.000 | 1.613 | 0.602 | 1.771 | 10.248 | 0.0244 | -0.387 | 59.01 | 4.642 | 3.893 | 0.748 |
| 48.75 | 5 | 2.236 | 1.688 | 0.699 | 1.710 | 9.750 | 0.0205 | -0.312 | 51.25 | 4.642 | 3.714 | 0.927 |
| 55.68 | 6 | 2.449 | 1.746 | 0.778 | 1.647 | 9.280 | 0.0180 | -0.254 | 44.32 | 4.642 | 3.539 | 1.103 |
| 62.83 | 7 | 2.646 | 1.798 | 0.845 | 1.570 | 8.976 | 0.0159 | -0.202 | 37.17 | 4.642 | 3.337 | 1.304 |
| 67.94 | 8 | 2.828 | 1.832 | 0.903 | 1.506 | 8.493 | 0.0147 | -0.168 | 32.06 | 4.642 | 3.177 | 1.465 |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 73.58 | 9 | 3.000 | 1.867 | 0.954 | 1.422 | 8.176 | 0.0136 | -0.133 | 26.42 | 4.642 | 2.978 | 1.663 |
| 81.06 | 10 | 3.162 | 1.909 | 1.000 | 1.277 | 8.106 | 0.0123 | -0.091 | 18.94 | 4.642 | 2.666 | 1.976 |
| 92.23 | 11 | 3.317 | 1.965 | 1.041 | 0.890 | 8.385 | 0.0108 | -0.035 | 7.77 | 4.642 | 1.981 | 2.661 |
| 99.83 | 12 | 3.464 | 1.999 | 1.079 | -0.770 | 8.319 | 0.0100 | -0.001 | 0.17 | 4.642 | 0.554 | 4.088 |

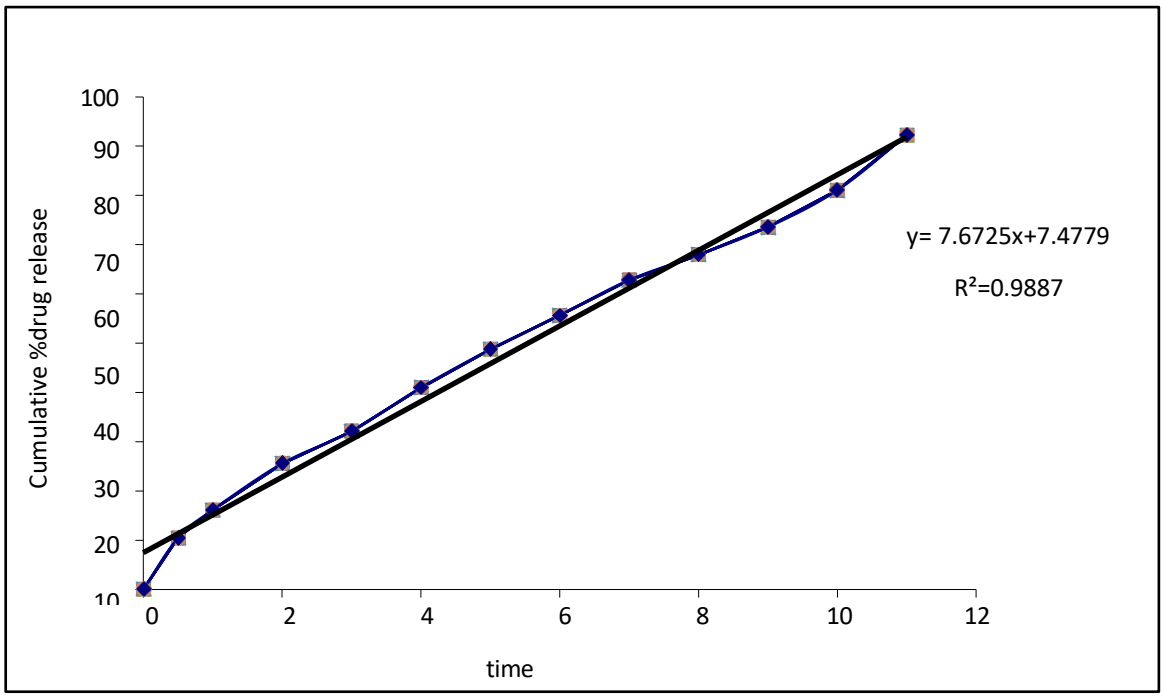


**Figure 5: Zero order release kinetics graph**

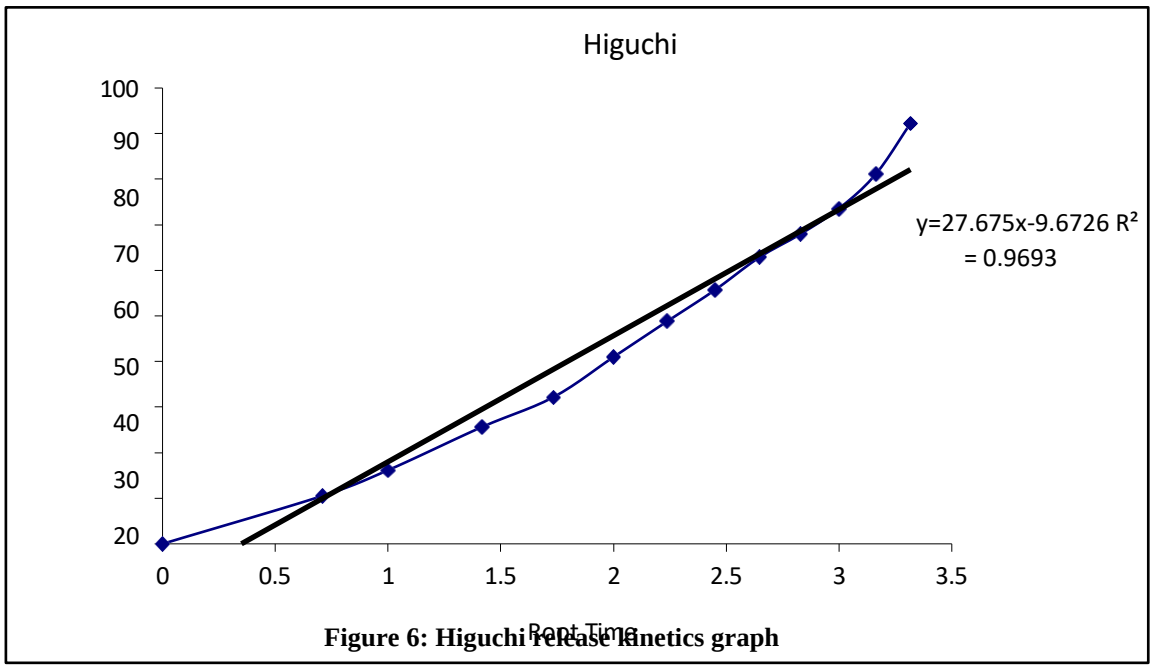


**Figure 6: Higuchi release kinetics graph**

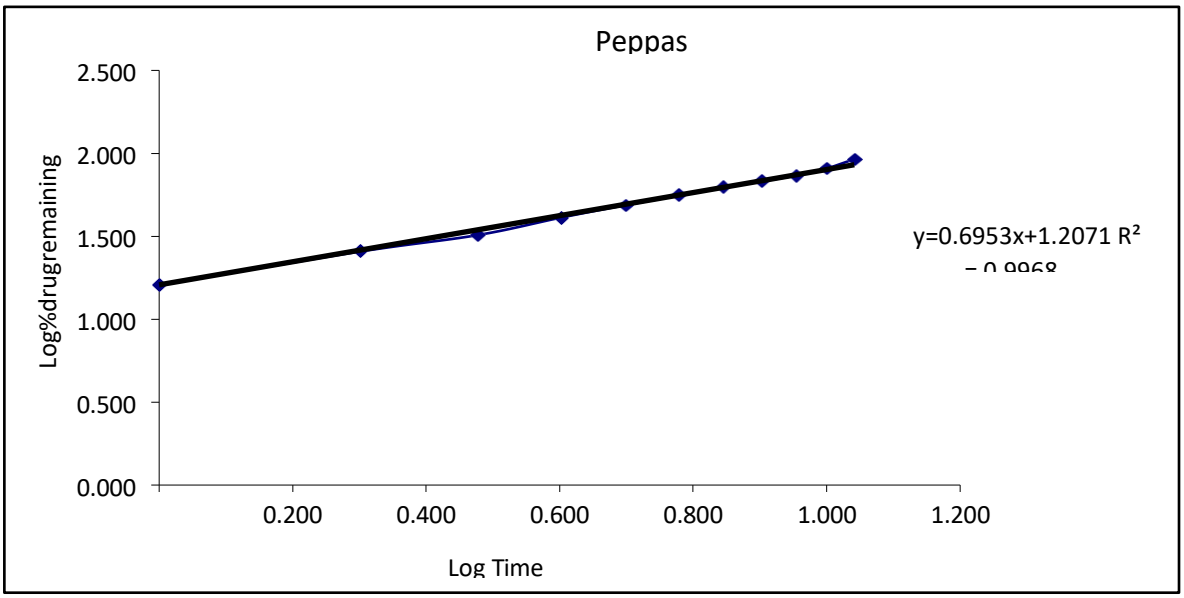


**Figure 7: Peppas release kinetics graph**

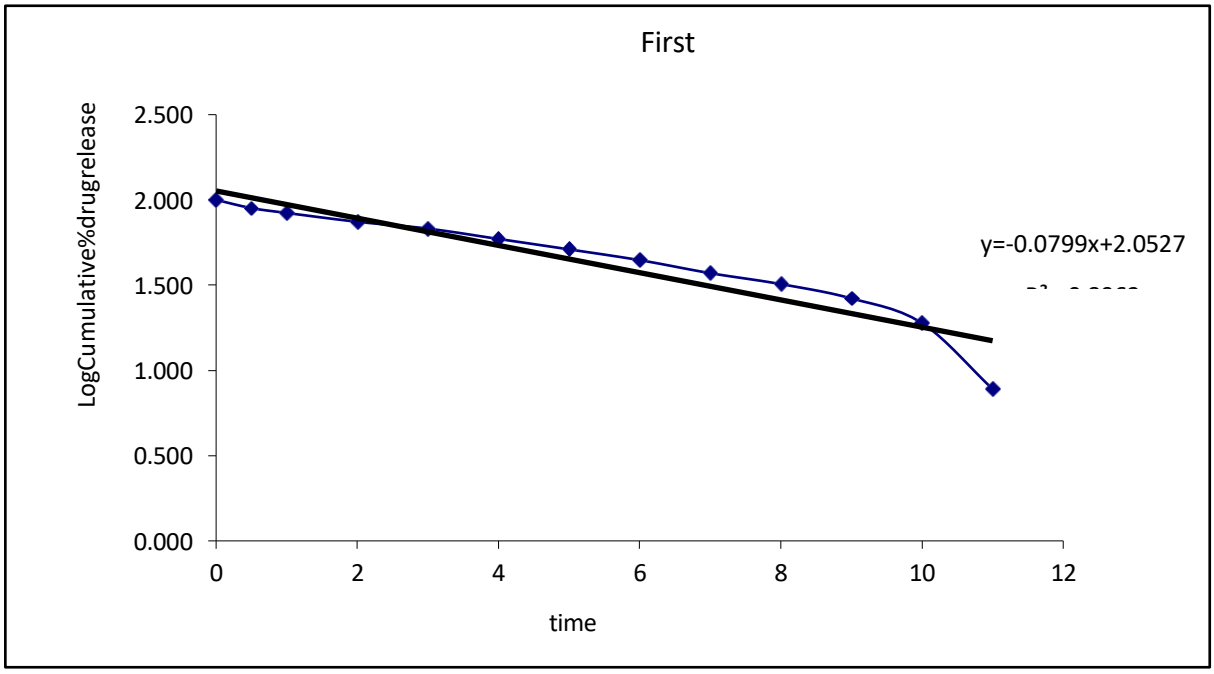


**Figure 8: First order release kinetics graph**

**Table 8: kinetics Correlation coefficient values**

| Release kinetics | Correlation coefficient values |
|---|---|
| Zero order release kinetics | $R^2 = 0.988$ |
| Higuchi release kinetics | $R^2 = 0.969$ |
| Peppas release kinetics | $R^2 = 0.996$ |
| First order release kinetics | $R^2 = 0.896$ |

From the above graphs it was evident that the formulation D3 was followed Peppas release mechanism.

**Drug – Excipient compatibility studies**

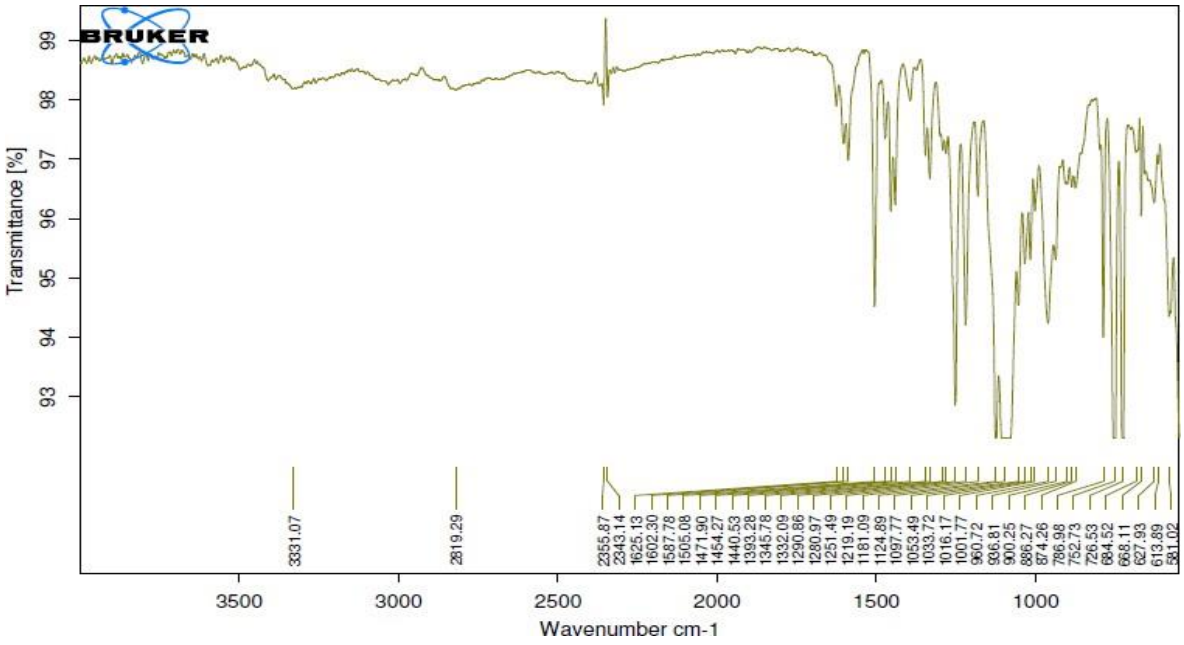


**Figure 9: FT-TR Spectrum of Dalfampridine pure drug**

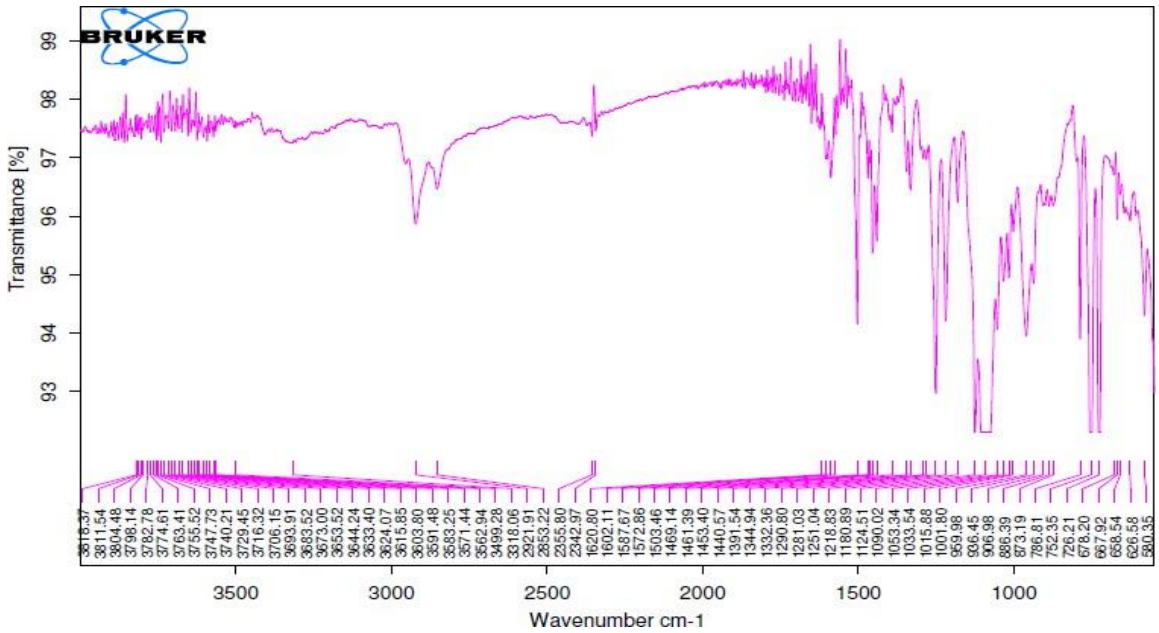


**Figure 10: FT-IR Spectrum of Optimised Formulation**

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 Dalfampridine and excipients used in the preparation of different Dalfampridine Sustained release formulations. Therefore the drug and excipients are compatible to form stable. Formulations under study. The FTIR spectra of Dalfampridine and physical mixture used for optimized formulation were obtained and these are depicted in above figures. From the FTIR data it was evident that the drug and excipients doses not have any interactions. Hence they were compatible.

## CONCLUSION:

Various dalfampridine formulations were developed by using release rate controlling and gel forming polymers like Tragacanth, Acacia gum and Xanthan gum in single by direct compression method. The active pharmaceutical ingredient Dalfampridine was evaluated for its physical characteristics, analytical profiles and drug polymer compatibility study. Result of the present study demonstrated that natural polymers could be successfully employed for formulating sustained release matrix tablets of Dalfampridine. In present studies, D3 formulation containing Tragacanth 30mg is probably showing release up to 99.83% within 12 hrs. According to drug release study it was found that there D3 formulation was showed maximum % of drug release in desired period of time and it is considered as optimized formulation (D3).

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