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# Formulation and Evaluation of Sustained Release Matrix Tablets of Methylphenidate

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## ABSTRACT

The Present work at investigating different polymers like Xanthan Gum, Guar Gum, Karaya Gum is an attempt to formulate sustained release matrix tablets containing Methylphenidate. Methylphenidate drug has short half -life makes the development of sustained release forms extremely advantageous. The standard curve of Methylphenidate was prepared in 01 N HCL and 6.8 Phosphate buffer at 258nm. The Nine Formulations were developed by the direct compression method. The in vitro drug release studies were carried out using USP type II apparatus i.e Paddle type. All the pre-compression and post compression parameters are within the limits as IP. The in vitro drug release F4 formulation showed good drug release i.e 99.92 %. The F4 formulation was consider as optimized Formulation.

**Keywords:** Methylphenidate, sustained release Matrix Tablets.

## INTRODUCTION

Sustained release dosage forms are designed to release a drug at a predetermined rate by maintaining a constant drug level for a specific period of time with minimum side effects. The basic rationale of sustained release drug delivery system optimizes the biopharmaceutical, pharmacokinetic and pharmacodynamics properties of a drug in such a way that its utility is maximized, side-effects are reduced and cure/treatment of the disease is achieved Introduction of matrix tablet as sustained release (SR) has given a new. Breakthrough for novel drug delivery system (NDDS) in the field of pharmaceutical technology. It excludes complex production procedures such as coating and pelletization during manufacturing and drug release rate from the dosage form is controlled mainly by the type and proportion of polymer used in the preparations. Hydrophilic polymer matrix is widely used for formulating an SR dosage form. Oral sustained release (SR) products provide an advantage over conventional dosage forms by optimizing bio-pharmaceutics, pharmacokinetics and pharmacodynamics properties of drugs in such a way that it reduce dosing frequency to an extent that once daily dose is sufficient for penetration, polymer swelling, drug dissolution, drug diffusion and matrix erosion . The materials most widely

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used in preparing matrix systems include both hydrophilic and hydrophobic polymers. Commonly available hydrophilic polymers include Hydroxypropylmethylcellulose (HPMC), Hydroxypropylcellulose (HPC), Hydroxyethyl cellulose (HEC), Xanthan gum, Sodium alginate, Poly (ethylene oxide) and cross-linked homopolymers and 3 copolymers of acrylic acid.[7,8,9,10]

## The following are the rationale of developing SR [11-14]

1) To extend the duration of action of the drug
2) To reduce the frequency of dosing
3) To minimize the fluctuations in plasma level
4) Improved drug utilization
5) Less adverse effects

## Advantages of sustained release dosage forms

1. The frequency of drug administration is reduced.
2. Patient compliance can be improved.
3. Drug administration can be made more convenient as well.
4. The blood level oscillation characteristic of multiple dosing of conventional dosage forms is reduced.
5. Better control of drug absorption can be attained, since the high blood level peaks that may be observed after administration of a dose of a high availability drug can be reduced.
6. The characteristic blood level variations due to multiple dosing of conventional dosage forms can be reduced.
7. The total amount of drug administered can be reduced, thus:
- Maximizing availability with minimum dose;
- Minimize or eliminate local side effects;
- Minimize or eliminate systemic side effects;
- Minimize drug accumulation with chronic dosing.
8. Safety margins of high potency drugs can be increased and the incidence of both local and systemic adverse side effects can be reduced in sensitive patients.
9. Improve efficiency in treatment.
- Cure or control condition more promptly
- Improve control of condition
- Improve bioavailability of some drugs
- Make use of special effects; e.g. sustain release aspirin for morning relief of arthritis by dosing before bed-time.
10. Economy

## Disadvantages of sustained release dosage forms

1) Probability of dose dumping.
2) Reduced potential for dose adjustment.
3) Cost of single unit higher than conventional dosage forms.
4) Increase potential for first pass metabolism.
5) Requirement for additional patient education for proper medication.
6) Decreased systemic availability in comparison to immediate release conventional dosage forms.
7) Poor invitro and invivo correlations.

## Aim of the Work

The aim of the study is to Formulation and Evaluation of Sustained Release Matrix Tablets of Methylphenidate

## Objective of the Study

Methylphenidate is a central nervous system stimulant. It affects chemicals in the brain and nerves that contribute to hyperactivity and impulse control. Methylphenidate is used to treat attention deficit disorder (ADD), attention deficit hyperactivity disorder (ADHD), and narcolepsy. The main objective of this study is to extend the drug release there by reducing the frequency of dosage.

## Formulation development of Tablets

All the formulations were prepared by direct compression. The compositions of different formulations are given in Table 1.The tablets were prepared as per the procedure given below and aim is to prolong the release of Methylphenidate. Total weight of the tablet was considered as 120mg.

**Table 1 : Formulation composition for tablet**

| INGREDIENTS | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| Methylphenidate | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| Xanthan Gum | 10 | 20 | 30 | - | - | - | - | - | - |
| Guar Gum | - | - | - | 10 | 20 | 30 | - | - | - |
| Karaya Gum | - | - | - | - | - | - | 10 | 20 | 30 |
| PVP K30 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| Talc | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Magnesium striate | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Lactose | 80 | 70 | 60 | 80 | 70 | 60 | 80 | 70 | 60 |
| Total weight | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 | 120 |

## RESULTS AND DISCUSSION

### Analytical Method

Graphs of Methylphenidate were taken in 0.1N HCl and in pH 6.8 phosphate buffer at 258 nm and 260nm respectively.

**Table 2: Observations for graph of Methylphenidate in 0.1N HCl (258 nm)**

| Conc [µg/ml] | Absorbance |
|---|---|
| 0 | 0 |
| 10 | 0.161 |
| 20 | 0.348 |
| 30 | 0.527 |
| 40 | 0.711 |
| 50 | 0.894 |

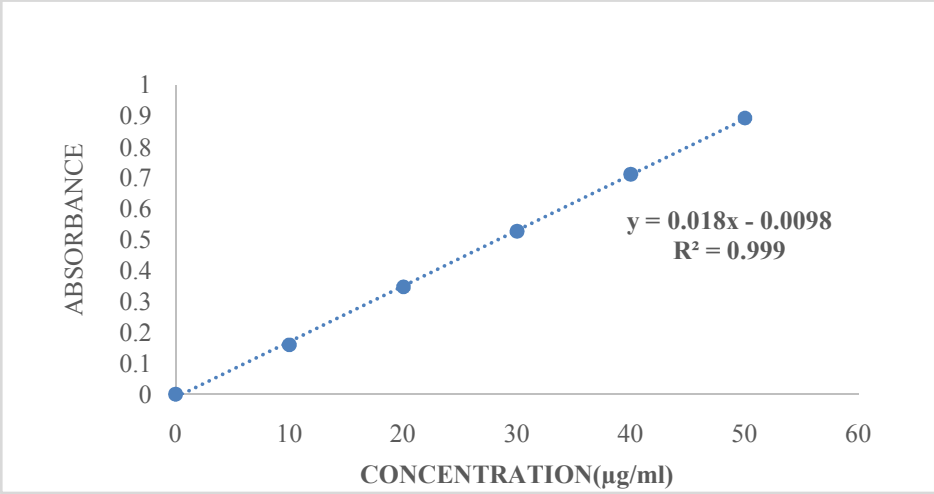


**Figure 1: Standard graph of Methylphenidate in 0.1N HCl**

**Table 3: Observations for graph of Methylphenidate in pH 6.8 phosphate buffer (260nm)**

| Concentration [µg/ml] | Absorbance |
|---|---|
| 0 | 0 |
| 10 | 0.138 |
| 20 | 0.301 |
| 30 | 0.465 |
| 40 | 0.627 |
| 50 | 0.818 |

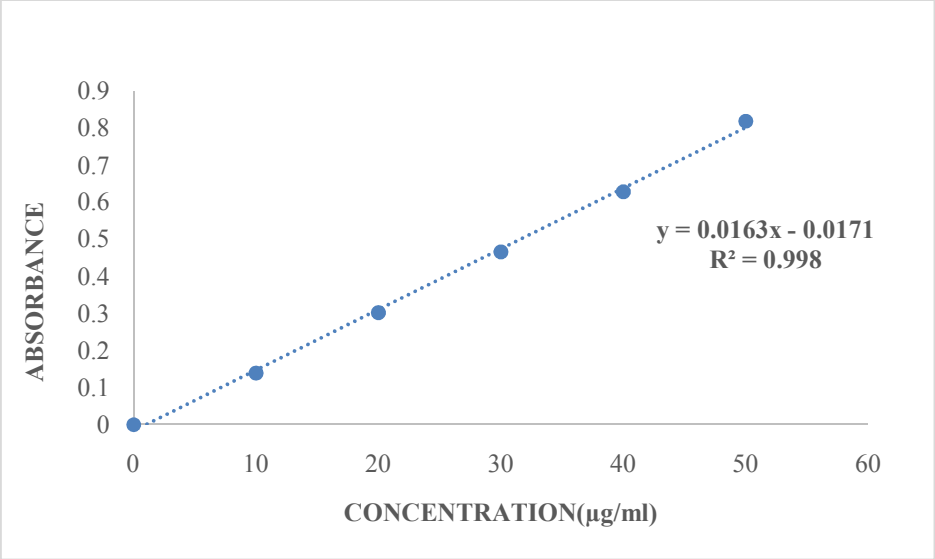


**Figure 2: Standard graph of Methylphenidate pH 6.8 phosphate buffer (260nm)**

**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 |
|---|---|---|---|---|---|
| **F1** | 29.12 | 0.32 | 0.36 | 12.66 | 1.15 |
| **F2** | 29.19 | 0.33 | 0.38 | 13.14 | 1.15 |
| **F3** | 28.73 | 0.46 | 0.53 | 13.53 | 1.16 |
| **F4** | 28.27 | 0.39 | 0.45 | 12.46 | 1.15 |
| **F5** | 26.91 | 0.39 | 0.45 | 12.84 | 1.15 |
| **F6** | 29.51 | 0.36 | 0.41 | 12.42 | 1.14 |
| **F7** | 27.34 | 0.37 | 0.42 | 11.61 | 1.13 |
| **F8** | 27.64 | 0.34 | 0.39 | 12.24 | 1.14 |
| **F9** | 27.57 | 0.35 | 0.40 | 11.86 | 1.13 |

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 of 0.32 to 0.46 (gm/cm3) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.36 to 0.53 showing the powder has good flow properties. The compressibility index of all the formulations was found to be below 19.47 which show that the powder has good flow properties.All

the formulations has shown the Hausner's ratio below 1.24 indicating the powder has good flow properties.

## Quality Control Parameters For tablets:

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

**Table 5: *In-vitro* quality control parameters for tablets**

| Formulation codes | Average weight(mg) | Hardness(kg/cm2) | Friability (%loss) | Thickness (mm) | Drug content (%) |
|---|---|---|---|---|---|
| F1 | 118.26 | 2.63±0.17 | 0.27 | 1.24±0.45 | 99.32 |
| F2 | 119.35 | 2.84±0.67 | 0.34 | 1.12±0.3 | 97.54 |
| F3 | 121.41 | 2.77±0.22 | 0.31 | 1.18±28 | 98.27 |
| F4 | 120.22 | 2.54±0.64 | 0.24 | 1.16±0.49 | 99.64 |
| F5 | 123.76 | 2.81±0.38 | 0.38 | 1.23±0.27 | 99.58 |
| F6 | 117.27 | 2.66±0.48 | 0.410.71 | 1.24±0.35 | 97.37 |
| F7 | 119.64 | 2.75±0.34 | 0.35 | 1.18±0.87 | 97.22 |
| F8 | 120.86 | 2.84±0.28 | 0.39 | 1.16±0.68 | 98.27 |
| F9 | 118.29 | 2.71±0.12 | 0.27 | 1.21±0.22 | 99.48 |

## Weight variation test

Tablets of each batch were subjected to weight variation test, difference in weight and percent deviation was calculated for each tablet and was shown in the Table 8.4. The average weight of the tablet is approximately in range of 117.27 to 123.76mg, so the permissible limit is ±7.5% (>200 mg). The results of the test showed that, the tablet weights were within the pharmacopoeia limit.

## Hardness test:

Hardness of the three tablets of each batch was checked by using Pfizer hardness tester and the data's were shown in Table 8.4. The results showed that the hardness of the tablets is in range of 2.63±0.17 to 2.84±0.67 kg/cm$^2$,which was within IP limits.

## Thickness

Thickness of three tablets of each batch was checked by using Micrometer and data shown in Table-8.4. The result showed that thickness of the tablet is raging from 1.16±0.49 to 1.24±0.45mm.

## Friability

Tablets of each batch were evaluated for percentage friability and the data were shown in the Table 8.4. 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 97.22 - 99.64%. 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 Methylphenidate Tablets Prepared with Xanthan Gum**

| *TIME* (hr) | CUMULATIVE PERCENT DRUG DISSOLVED | | |
|---|---|---|---|
| | F1 | F2 | F3 |
| **0** | 0 | 0 | 0 |
| **0.5** | 9.12 | 14.49 | 16.41 |
| **1** | 15.33 | 19.73 | 22.32 |

| | | | |
|---|---|---|---|
| **2** | 21.46 | 24.53 | 27.63 |
| **3** | 28.18 | 31.65 | 33.94 |
| **4** | 34.67 | 36.47 | 38.26 |
| **5** | 41.89 | 39.15 | 42.82 |
| **6** | 45.77 | 44.24 | 51.23 |
| **7** | 52.58 | 47.94 | 59.14 |
| **8** | 57.37 | 53.31 | 66.44 |
| **9** | 63.73 | 58.22 | 71.02 |
| **10** | 69.24 | 67.08 | 82.63 |
| **11** | 76.62 | 79.73 | 86.15 |
| **12** | 84.91 | 87.18 | 91.23 |

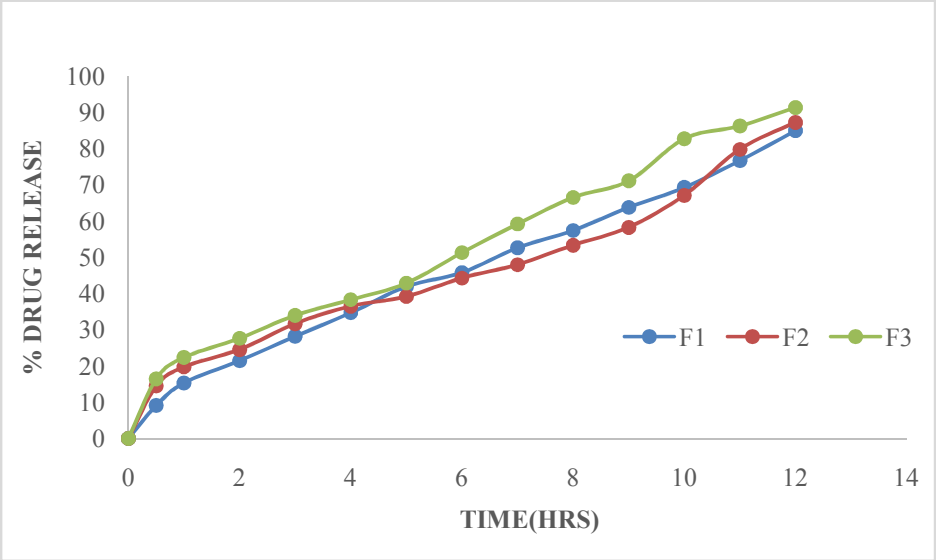


**Fig 3: Dissolution profile of Methylphenidate (F1-F3 formulations).**

**Table 7: Dissolution Data of Methylphenidate Tablets Prepared With Guar Gum**

| ***TIME*** **(hr)** | **CUMULATIVE PERCENT DRUG DISSOLVED** **F4** | **F5** | **F6** |
|---|---|---|---|
| 0 | 0 | 0 | 0 |
| 0.5 | 18.85 | 20.13 | 23.66 |
| 1 | 25.62 | 27.44 | 29.13 |
| 2 | 36.21 | 34.56 | 36.87 |
| 3 | 39.58 | 41.47 | 43.64 |
| 4 | 44.78 | 49.88 | 47.51 |
| 5 | 53.19 | 56.96 | 54.72 |
| 6 | 62.73 | 64.25 | 62.83 |
| 7 | 67.54 | 72.88 | 68.75 |
| 8 | 73.05 | 76.74 | 74.62 |
| 9 | 84.29 | 81.54 | 79.05 |
| 10 | 89.55 | 86.26 | 83.12 |
| 11 | 92.81 | 93.08 | 88.54 |
| 12 | 99.92 | 96.43 | 94.87 |

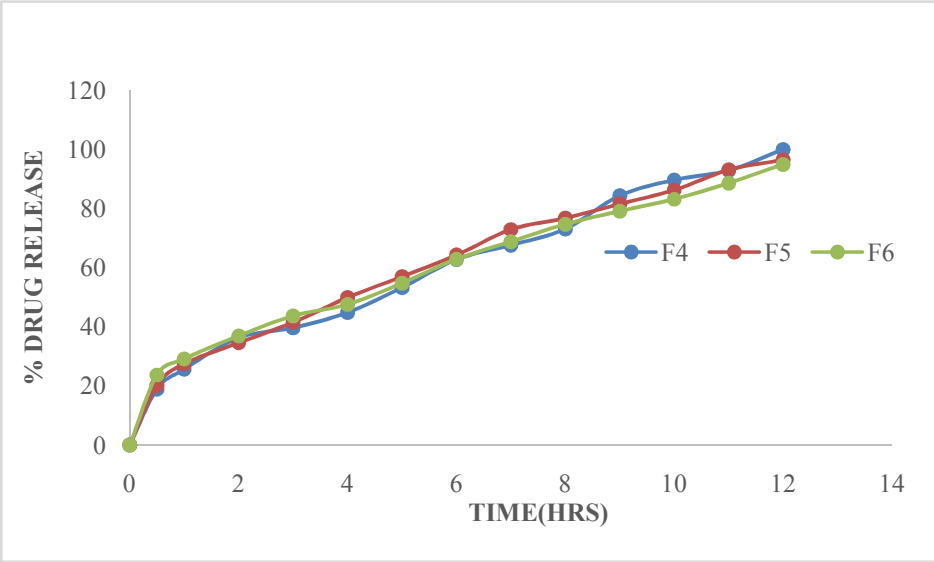


**Fig 4: Dissolution profile of Methylphenidate (F4- F6 formulations)**

**Table 8: Dissolution Data of Methylphenidate Tablets Prepared With Karaya gum**

| *TIME* (hr) | CUMULATIVE PERCENT DRUG DISSOLVED | | |
|---|---|---|---|
| | F7 | F8 | F9 |
| 0 | 0 | 0 | 0 |
| 0.5 | 19.32 | 24.43 | 26.17 |
| 1 | 23.93 | 28.08 | 31.62 |
| 2 | 29.27 | 33.84 | 35.41 |
| 3 | 34.68 | 36.19 | 44.07 |
| 4 | 41.16 | 42.22 | 52.42 |
| 5 | 45.34 | 48.76 | 57.36 |
| 6 | 49.89 | 55.78 | 63.94 |
| 7 | 53.27 | 62.59 | 68.51 |
| 8 | 58.06 | 68.44 | 73.79 |
| 9 | 66.28 | 72.26 | 76.48 |
| 10 | 74.86 | 79.45 | 82.27 |
| 11 | 78.04 | 83.69 | 85.43 |
| 12 | 92.57 | 89.27 | 88.31 |

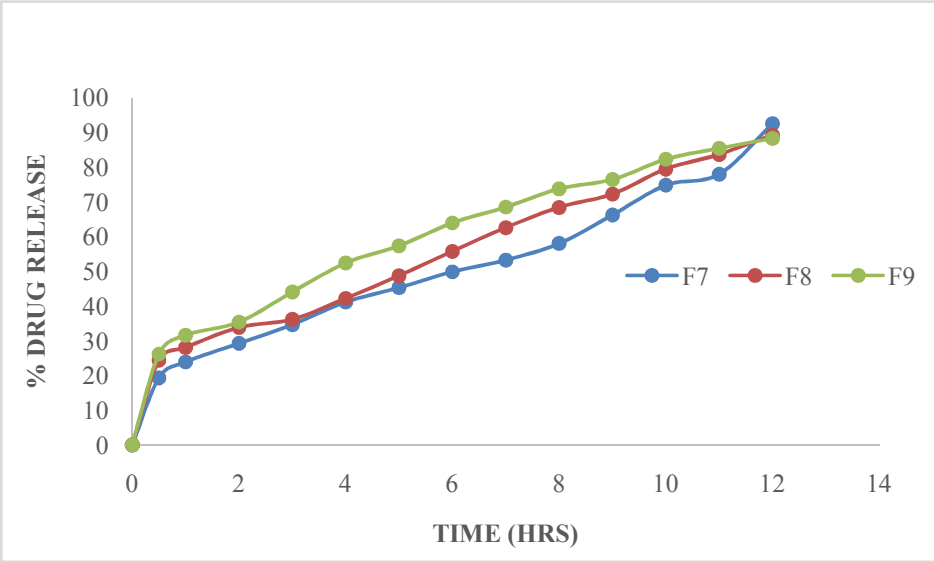


**Fig 5: Dissolution profile of Methylphenidate (F7- F9 formulations)**

From the dissolution data it was evident that the formulations prepared with Xanthan Gumas polymer were retard the drug release up to desired time period i.e., 12 hours and showed maximum of (F3) 91.23% in 12 hours with good retardation. Formulations prepared with Guar Gum retarded the drug release in the concentration of 10 mg (F4 Formulation) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 99.92 % in 12 hours with good retardation. Formulations prepared with Karaya gum retarded the drug release in the concentration of 10 mg (F7Formulation) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 92.57% in 12 hours with good retardation. From the above results it was evident that the formulation F4 is best formulation with desired drug release pattern extended up to 12 hours.

**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.

**Table 9: Release Rate Kinetics to Dissolution Data**

| TIME ( T ) | ROOT (T) | LOG( %) RELEASE | LOG ( T ) | LOG (%) REMAIN | RELEASE RATE (CUMULATIVE % RELEASE / t) | 1/CUM% RELEASE | PEPPAS log Q/100 | % Drug Remaining | Q01/3 | Qt1/3 | Q01/3-Qt1/3 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 0 | | | 2.000 | | | | 100 | 4.642 | 4.642 | 0.000 |
| **0.5** | 0.707 | 1.270 | -0.301 | 1.911 | 18.85 | 0.0538 | -0.730 | 81.4 | 4.642 | 4.334 | 0.308 |
| **1** | 1.000 | 1.433 | 0.000 | 1.863 | 25.62 | 0.0369 | -0.567 | 72.9 | 4.642 | 4.177 | 0.464 |
| **2** | 1.414 | 1.535 | 0.301 | 1.818 | 36.21 | 0.0292 | -0.465 | 65.7 | 4.642 | 4.035 | 0.606 |
| **3** | 1.732 | 1.668 | 0.477 | 1.728 | 39.58 | 0.0215 | -0.332 | 53.4 | 4.642 | 3.766 | 0.876 |
| **4** | 2.000 | 1.713 | 0.602 | 1.685 | 44.78 | 0.0194 | -0.287 | 48.4 | 4.642 | 3.644 | 0.997 |
| **5** | 2.236 | 1.777 | 0.699 | 1.604 | 53.19 | 0.0167 | -0.223 | 40.2 | 4.642 | 3.426 | 1.216 |
| **6** | 2.449 | 1.822 | 0.778 | 1.526 | 62.73 | 0.0151 | -0.178 | 33.6 | 4.642 | 3.227 | 1.415 |
| **7** | 2.646 | 1.862 | 0.845 | 1.435 | 67.54 | 0.0137 | -0.138 | 27.2 | 4.642 | 3.007 | 1.634 |
| **8** | 2.828 | 1.903 | 0.903 | 1.303 | 73.05 | 0.0125 | -0.097 | 20.1 | 4.642 | 2.719 | 1.923 |
| **9** | 3.000 | 1.931 | 0.954 | 1.167 | 84.29 | 0.0117 | -0.069 | 14.7 | 4.642 | 2.450 | 2.192 |
| **10** | 3.162 | 1.967 | 1.000 | 0.869 | 89.55 | 0.0108 | -0.033 | 7.4 | 4.642 | 1.949 | 2.693 |
| **11** | 3.317 | 1.982 | 1.041 | 0.613 | 92.81 | 0.0104 | -0.018 | 4.1 | 4.642 | 1.601 | 3.041 |
| **12** | 3.464 | 1.988 | 1.079 | 2.000 | 99.92 | 0.0106 | | 100 | 4.642 | 4.642 | 0.000 |

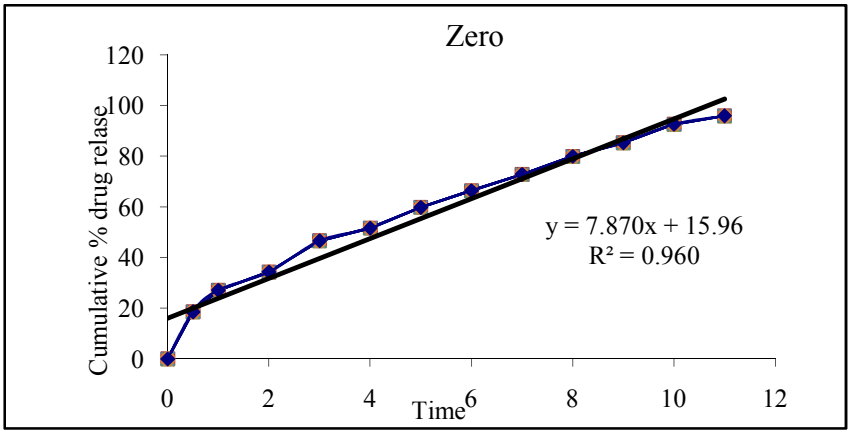


**Fig 6 : Zero order release kinetics graph**

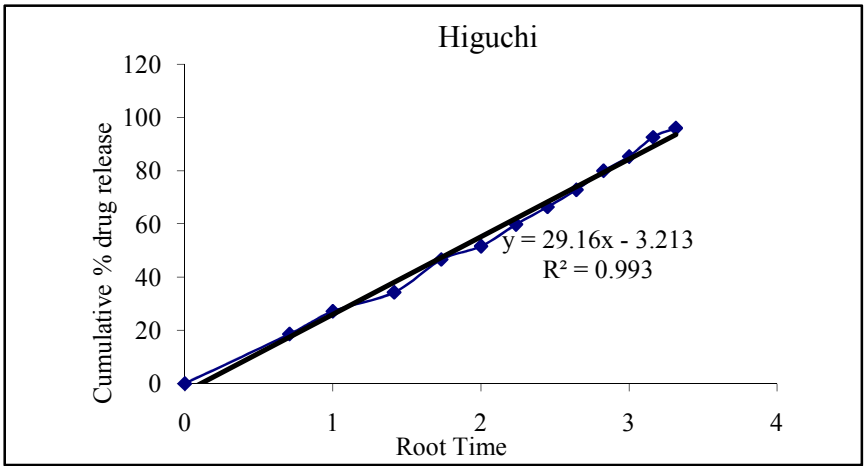


**Fig 7: Higuchi release kinetics graph**

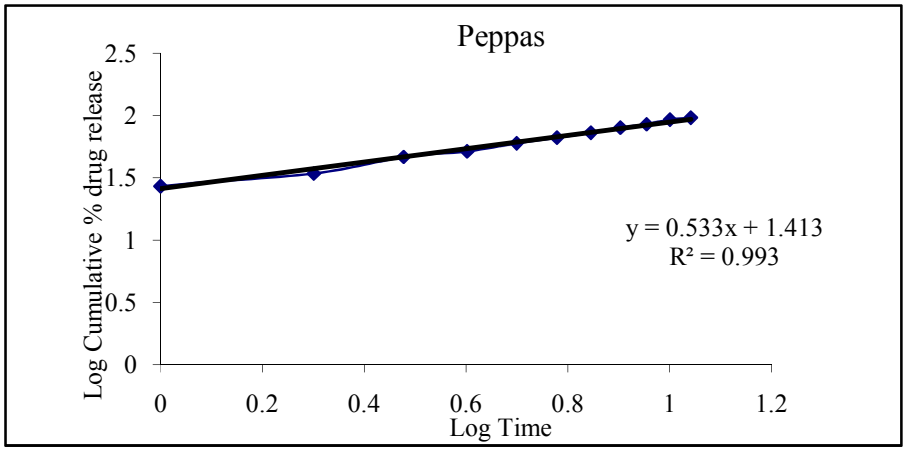


**Fig 8: Kars mayer peppas graph**

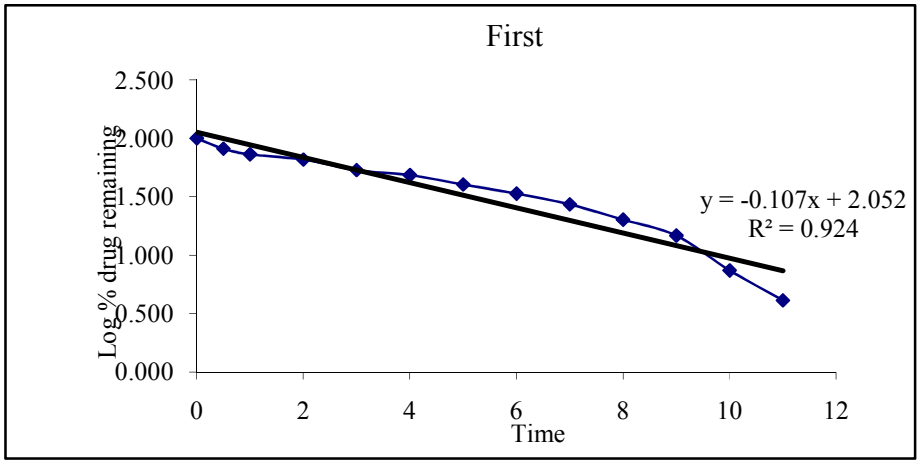


**Fig 9: First order release kinetics graph**

From the above graphs it was evident that the formulation F4 was followed Higuchi release kinetics.

**Drug – Excipient compatibility studies**
**Fourier Transform-Infrared Spectroscopy**

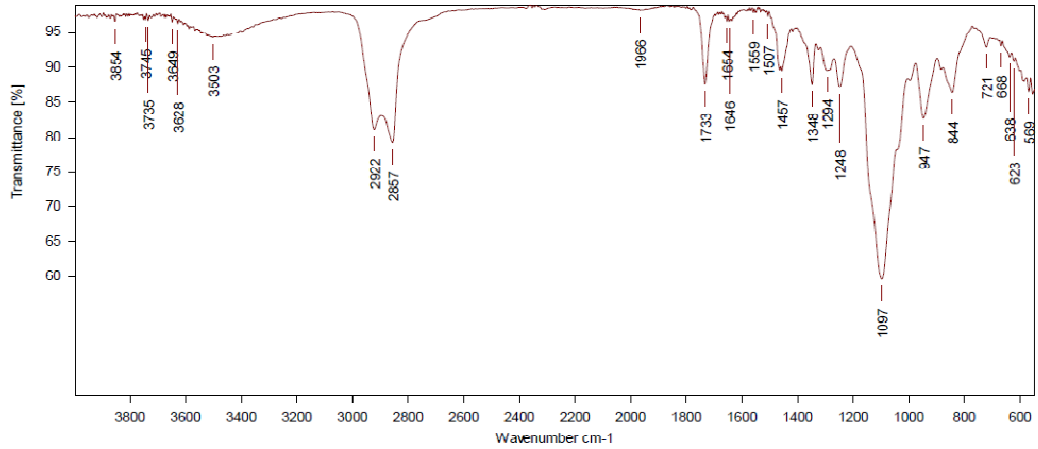


**Figure 10: FT-TR Spectrum of Methylphenidate pure drug.**

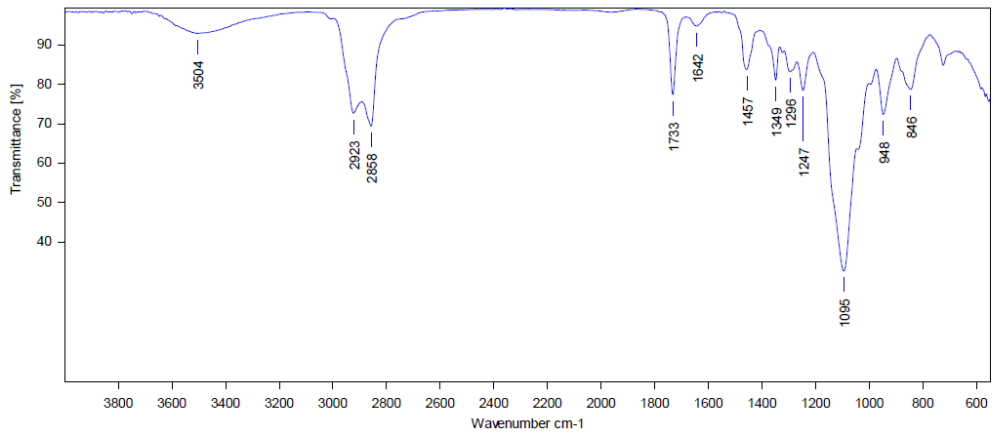


**Figure 11: FT-IR Spectrum of Optimized Formulation**

## CONCLUSION

Development of sustained release matrix tablets of Methylphenidate can be prepared because extended release formulation can reduce frequency of dose administration can reduce side effects and improve patient compliance. There for in the present study matrix tablets of Methylphenidate were prepared by using different polymers with different ratios by direct compression method. All the Evaluation parameters are in the limits. F4 formulation was consider as a optimized formulation it shows good drug release.

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