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RESEARCH ARTICLE

# Formulation and Evaluation of Nicorandil Sustained Release Matrix Tablets Using Natural Gum Mangifera Indica as Release Modifier

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**ABSTRACT**

The purpose of the present study was to formulate the nicorandil sustained release matrix tablets by using Mangifera indica gum as rate controlling factor and to evaluate drug release parameters as per various release kinetic models. The Mangifera indica gum is extracted and evaluated for physicochemical and phytochemical property using official procedures. The tablets were prepared by wet granulation method. The granules were evaluated for angle of repose, loose bulk density, tapped bulk density and compressibility index, showed satisfactory results. All the granules were lubricated and compressed and were evaluated for uniformity of weight, content of active ingredient, thickness, friability, hardness and In-vitro dissolution studies. Fourier transform infrared (FTIR) study revealed that there was no chemical interaction between drug and the gum used. All the formulation showed compliance with Pharmacopoeial standards. In-vitro drug release studies were carried out using USP 35/NF 30 dissolution apparatus type II at 50 rpm (rate per minute). The in-vitro release study of matrix tablets were carried out for 12 h. The prepared matrix tablets were shown 97.8%, 96.5%, 96.8%, 90.7% and 86.5% release over a period of 12 h. A better sustained drug release of 96.8% was obtained with formulation F3 at the end of 12 h. Optimized formulation F3 was subjected to stability studies for three months, which showed stability with respect to release pattern. Mathematical analysis of the release kinetics indicated that the nature of drug release from the matrix tablets was dependent on gum concentration and it was found to be diffusion coupled with erosion.

**Keywords:** Sustained release, *Mangifera indica*, Matrix tablets, Nicorandil.

## 1. INTRODUCTION

The oral route is the route most often used for administration of drugs. Tablets are the most popular oral formulations available in the market and are preferred by patients and physicians alike. In long-term therapy for the treatment of chronic disease conditions, conventional formulations are required to be administered in multiple doses and therefore have several disadvantages[1]. Sustained release tablet formulations are preferred for such therapy because they offer better patient compliance, maintain uniform drug levels, reduce dose and side effects, and increase the safety margin for high-potency drugs[2].

Various types of oral sustained release formulations have been developed to improve the clinical efficacy of drugs having short half-lives as well as to increase patient compliance[3]. These formulations are designed to deliver drugs at a predetermined rate over a wide range of conditions and durations of therapeutic treatments. One of the most commonly used methods of developing controlled release formulations for therapeutic agents is to include it in matrix tablets, as they are easy to manufacture[4]. Using a suitable rate controlling gum, the matrix can be tableted by direct compression or conventional wet granulation method. Because of their simplicity and cost effectiveness, natural gums can be



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used extensively for oral sustained release dosage forms. Hydration of natural gum results in the formation of a gel layer that controls the release rate of the drug. In-vitro drug release of water soluble drug is controlled by diffusion out of the gel layer at a rate controlled by the gel viscosity, whereas release for poorly soluble drug is solely by dissolution[5].

Nicorandil, a drug approved for the treatment of ischemic heart disease, is believed to have dual properties. The intrinsic mechanism of the drug (selective activation of $K^+_{ATP}$channels at the sarcolemmal and mitochondrial level) allows coronary and peripheral vasodilatation with subsequent reduction of preload and after load. Secondly, because of the role $K^+_{ATP}$channels in ischemic preconditioning, nicorandil have been attributed cardio protective effects[6].

Nicorandil is soluble in water, freely soluble in acetone, methanol, and ethanol. Nicorandil is eliminated by plasma with a half-life of approximately 1 h. The total body clearance of nicorandil is less than the liver blood flow. After metabolism the nicorandil is converted primarily to the de-nitrated compound, SG-86(N-2-hydroxyethyl nicotinamide), which is pharmacologically inactive. The urinary excretion and the alcohol metabolite accounted for 1% and 4% of the dose (single 20 mg dose) in 24 h, respectively[7].

However, developing oral controlled release tablets for water-soluble drugs with constant release rate has always been a challenge to the pharmaceutical technologist. Most of these water-soluble drugs, if not formulated properly, may readily release the drug at a faster rate and produce a toxic concentration of the drug on oral administration. In recent years, considerable attention has been focused on hydrophilic polymers in the design of oral sustained release drug delivery systems because of their flexibility to obtain a desirable drug release profile, cost-effectiveness, and broad regulatory acceptance. Among the hydrophilic polymers, cellulose derivatives such as methyl cellulose, hydroxylpropyl methylcellulose, and sodium carboxymethyl cellulose are generally considered to be stable and safe as release retardant excipients in the development of oral sustained release dosage forms. These semi-synthetic polymers are quite expensive when compared with natural gums such as *Mangifera indica* gum (mangifera gum). The natural gums are nontoxic and easily available. The objective of the present investigation was to develop oral controlled release tablets for water soluble nicorandil using a natural gum obtained from *Mangifera indica* [8].

*Mangifera indica* tree belongs to genus Mangifera of the family Anacardiaceae. The trees have been grown throughout the tropical and subtropical world for thousands of years and have become an integral part of many cultures. *Mangifera indica* grows up to 35m to 40 m tall; with a crown radius of 10 m .The trees are long-lived, as some specimens still fruit after 300 years. It is used in folk medicine by various people for natural remedy against chronic dysentery, prevention/protection of cancer, scabies, asthma, anti bacterial activity. The bark exudates yield resin, gum, ash, and tannins[9-11].

In the present work, we have isolated and characterized *Mangifera indica* gum and evaluated its sustained release properties employing nicorandil as a model drug. The matrix tablet of nicorandil was formulated and evaluated for Pre and Post compression parameters.

## 2. MATERIALS AND METHODS

Nicorandil was obtained as a gift sample from Gayatri Pharmachem, Rankanpur. Mangifera resin gum was collected from the incised trunk of *Mangifera indica* tree in Tumkur region. PVP K 30, Talc and Magnesium stearate from LobaChem(Mumbai, India). All other chemicals and ingredients were used for study are of Analytical grade.

### 2.1. Extraction of *Mangifera indica* Gum

The Mangifera resin gum was collected from *Mangifera indica* trees (injured trunk site). It was dried, milled and passed through sieve no 80. Dried gum was stirred in distilled water for 6-8 h at room temperature. The supernatant was obtained by centrifugation. The residue was washed with water and the washings were added to separate supernatant. The procedure was repeated four more times. Finally the supernatant was made up to 500 ml and treated with twice the volume of acetone by continuous stirring. The precipitated material was washed with acetone and dried at 50-60°C under vacuum. The dried gum was pulverized and stored in tightly closed container[12-13].

### 2.2. Physicochemical properties of Mangifera gum

The physicochemical properties such as visual identification, solubility, pH, Ash value, and loss on drying, pre-compression parameters and microbial load of the mangifera gum were determined according to official Procedures[14-17]. The following evaluation parameters were presented, see Table 2.

### 2.3. Phytochemical properties of Mangifera gum

Preliminary tests were performed to confirm the nature of gum obtained. The chemical tests are conducted for carbohydrates, tannins, alkaloids, proteins, glycosides, flavanoids, reducing sugars[18]. The result of the phytochemical examination were presented, see Table 3.

### 2.4. Characterization of Drug and Excipients using Fourier transform infra red spectroscopy (FTIR)

FTIR spectra of pure Nicorandil, Mangifera gum and physical mixture of drug and excipients were recorded on Shimadzu Corporation, (Tokyo, Japan) Model-1601 PC. Fourier transform-infra red: The Fourier transform-infrared (FT-IR) spectrum of the sample was recorded in



 

an IR spectrometer using potassium bromide (KBr) discs prepared from powdered samples mixed with dry KBr in the ratio 1:200. Triplicate measurements were made, and the spectrum with the clearest identifiable peaks was chosen.

**2.5. Preparation of Nicorandil Matrix Tablets**

Matrix tablets were prepared by wet granulation method. The composition of various formulations is given, see Table 1. Nicorandil, Mangifera gum and Lactose were mixed in a polybag and the mixture was passed through mesh (No.60). Granulation was done using a solution of PVP- K-30 in sufficient isopropyl alcohol. The wet mass passed through mesh No.16. The wet granules were air dried for 2 h. The granules were then sized by mesh No.22 and mixed with magnesium stearate and talc. Tablets were compressed using rotary tablet machine with concave punch. Tablet weight was (150 mg) kept constant as shown in Table. Five different formulae, having different concentrations of mangifera gum (20, 25, 30, 35 and 40 mg per tablet), were developed to evaluate the drug release and to study the effect of mangifera gum concentration on drug release.

| Ingredients (mg) | F1 | F2 | F3 | F4 | F5 |
|---|---|---|---|---|---|
| Nicorandil | 20 | 20 | 20 | 20 | 20 |
| *Mangifera indica* | 20 | 25 | 30 | 35 | 40 |
| PVP K 30 | 5 | 5 | 5 | 5 | 5 |
| Talc | 6 | 6 | 6 | 6 | 6 |
| Magnesium stearate | 3 | 3 | 3 | 3 | 3 |
| Lactose monohydrate | 96 | 91 | 86 | 81 | 76 |

Total weight per tablet: 150 mg

**Table 1: Composition of different formulations**

**2.6. Pre compression parameters**

The prepared powder blend was evaluated for various parameters like angle of repose, loose bulk density, tapped bulk density, compressibility index[19-21].

**2.7. Post compression parameters**

All prepared matrix tablets were evaluated for its uniformity of weight, hardness, friability and thickness according to official methods. Tablet hardness was determined for 10 tablets using a Monsanto tablet hardness tester. Friability was determined by testing 20 tablets in a friability tester for 4 minutes at 25 rpm/min. The weight variation was determined by taking 20 tablets using an electronic balance[22].

***2.8. In-vitro* dissolution studies**

The release rate of Nicorandil from sustained matrix tablets were determined using USP dissolution testing apparatus II (paddle type) at 50 rpm. The dissolution test was performed using 750 ml of 0.1N HCl (pH 1.2) for 2 h at 37±0.5°C and then 250 ml of 0.2M trisodium phosphate ($Na_3PO_4.12H_2O$) was added and pH is adjusted to 6.8 as described in the USP 35/NF 30 general monograph. Dissolution test was carried out for a period of 12 h using, 0.1N HCl (pH 1.2) for first 2 h and then the pH is adjusted to 6.8 for the rest of the period. The temperature of the dissolution medium is maintained at 37±0.5°C. 10 ml of the sample was withdrawn at regular intervals and replaced with the same volume of fresh pre-warmed dissolution medium. After filtration, the drug release at different time intervals was measured using an ultraviolet visible spectrophotometer (Labindia, Mumbai, India) at 262 nm. The study was performed in triplicate[23].

**2.9. Drug release kinetics**

To study the release kinetics, data obtained from in-vitro drug release studies were plotted in various kinetic models: zero order (Equation 1) as cumulative amount of drug release vs time, first order (Equation 2) as log cumulative percentage of drug remaining vs time, and Higuchi's model (Equation 3) as cumulative percentage of drug released vs square root of time.

$$C=K0\ t \quad \text{..... (1)}$$

Where K0 is the zero order rate constant expressed in units of concentration / time and t is the time in hours. A graph of concentration vs time would yield a straight line with a slope equal to K0 and intercept the origin of the axes[24].

$$\log C = \log C0 - Kt/2.303 \quad \text{..... (2)}$$

Where C0 is the initial concentration of drug, K is the first order constant, and t is the time[25].

$$Q = kt^{1/2} \quad \text{..... (3)}$$

Where k is the constant reflecting the design variables of the system and t is the time in hours. Hence, drug release rate is proportional to the reciprocal of the square root of time[26].

Mechanism of drug release:

To evaluate the mechanism of drug release from nicorandil sustained release tablets, data of drug release were plotted in korsmeyer et al's equation (Equation 4) as log cumulative percentage of drug release vs log time and the exponent n was calculated through the slope of the straight line.

$$Mt/M\infty = ktn \quad \text{..... (4)}$$

Where $Mt/M\infty$ are the fractional solute release, t is the release time, k is a kinetic constant characteristics of the drug/polymer system, and n is an exponent that characterizes the mechanism of release of tracers. For cylindrical matrix tablets, if the exponent n=0.45, then the drug release mechanism is Fickian diffusion, and if $0.45 < n < 0.89$, then it is non-Fickian or anomalous diffusion. An exponent's value of 0.89 is indicative of case-II Transport or typical zero-order release[27-28].



 

**2.10. Stability Studies**

To assess the drug and formulation stability, stability studies were done according to ICH guidelines. The optimized formulation was subjected to stability study at 40±2ºC and 75±5% RH for 90 days. The samples were evaluated for physical changes, hardness, friability, drug content and percentage drug release during the stability studies[29-30].

**3. RESULTS AND DISCUSSION**

**3.1. Physicochemical properties mangifera gum**

The physicochemical parameters of mangifera gum were evaluated. The mangifera gum is slightly soluble in water, forms thick gel in water, practically insoluble in alcohol, acetone and chloroform. The moisture content of mangifera gum was low, suggesting its suitability in formulations containing moisture sensitive drugs. A 1% w/v solution of mangifera gum in water gave a pH of 6.6. Knowledge of the pH of excipients is an important parameter in determining its suitability in formulations since the stability and physiological activity of most preparations depends on pH.

The total ash and acid insoluble ash value of mangifera gum was found to be 2.32% and 0.35% w/w respectively. Ash values reflect the level of adulteration or handling of the drug. Adulteration by sand or earth is immediately detected as the total ash is normally composed of inorganic mixtures of carbonates, phosphates, silicates and silica. Therefore, the low values of total ash and acid insoluble ash obtained in this study indicate low levels of contamination during gathering and handling of crude mangifera gum. The bulk and tapped densities give an insight on the packing and arrangement of the particles and the compaction profile of a material. The compressibility index and angle of repose of mangifera gum was 9.6% and 21.24° respectively, implying that the mangifera gum has a good compressibility with moderate flow. The loss on drying, ash value and microbial count were well within official limits.

The mangifera gum physicochemical properties are presented, see Table 2.

**3.2. Phytochemical properties of mangifera gum**

Phytochemical tests carried out on mangifera gum confirmed the presence of mucilage giving positive result when treated with ruthenium red, it showed red colour confirming the obtained product as gum. Molisch's test gives positive with the formation of violet ring at the junction of two liquids, confirming the presence of carbohydrates. Mucilage could not reduce Fehling's solution, so the sugars present were non reducing sugars. The test confirmed the absence of alkaloids, glycosides and tannins. No blue colour obtained when the gum is treated with iodine indicating the absence of starch. The results of phytochemical properties of mangifera gum were summarized, see Table 3.

| **Parameters** | ***Mangifera indica*** |
|---|---|
| Solubility | Slightly soluble in water, forms thick gel in water. Practically insoluble in alcohol, chloroform and acetone. |
| Odor | No characteristic odor |
| Taste | Tasteless |
| Color | Off white- cream yellow color |
| State | Amorphous powder |
| pH (1% w/v solution) | 6.6 |
| Loss on drying | 1.40% |
| Ash value | 2.32% |
| Water soluble ash | 1.40% |
| Acid insoluble ash | 0.35% |
| Sulphated ash | 1.20% |
| **Swelling ratio** | |
| In water | 25 |
| In 0.1 N HCl | 20 |
| In phosphate Buffer 6.8 | 10 |
| Bulk density (g/ml) | 0.31 |
| Tapped density (g/ml) | 0.34 |
| Compressibity index (%) | 9.60 |
| Angle of repose | 21.24 |
| **Total bacterial count** | |
| E.coli | Absent |
| Salmonella typhi | Absent |
| S.aureus | Absent |
| Yield (%) | 42 |

**Table 2: Physicochemical properties of *Mangifera indica*.**

| **Tests Observation** | ***Mangifera indica*** |
|---|---|
| Test for Carbohydrates (Molisch's test) | + |
| Test for Tannins (Ferric chloride test) | - |
| Test for proteins (Ninhydrin test) | - |
| Test for alkaloids (Wagner's test) | - |
| Test for glycosides(Keller-Killaini test) | - |
| Test for mucilage ( Ruthenium red test) | + |
| Test for steroids (Salkowski test) | - |
| Test for flavonoids (Shinoda test) | - |
| Test for reducing sugar (Felhing's test) | - |
| Mounted in 95% alcohol | Translucent angular masses under microscope |
| Mounting in the iodine | No blue colored particles (starch absent) |
| Test for chlorides (silver nitrate test) | - |
| Test for sulphates (barium chloride test) | - |

**Table 3: Phytochemical properties of *Mangifera indica*.**



 

### 3.3. Characterization of Drug and Excipients

In order to determine possible interaction between the nicorandil drug, mangifera gum and other excipients used in the formulation, compatibility studies were conducted using FTIR spectroscopy. There was no significant shift in the positions of the wave numbers when compared to that of the pure drug values. Thus there was no interaction between the drug and other excipients of the formulation.

### 3.4. Pre compression parameters

Powder blend prepared for compression of matrix tablets were evaluated for their flow properties like angle of repose, loose bulk density, tapped bulk density and compressibility index. The results were shown, see Table 4. Angle of repose was in the range of 24.57±0.94 to 28.19±1.47. The loose bulk density of the granules was in the range of 0.2595±0.008 to 0.2751±0.012 gm/ml. The tapped bulk density was in the range of 0.2912±0.013 to 0.3123±0.011 gm/ml, which indicates that the granules were not bulky. The compressibility index was found to be in the range of 10.43 to 15.6.

| Parameters | F1 | F2 | F3 | F4 | F5 |
|---|---|---|---|---|---|
| Angle of repose (Θ) | 24.57± 0.94 | 27.63± 1.63 | 28.19± 1.47 | 25.75± 2.01 | 26.42± 1.28 |
| Loose bulk density LBD (g/ml) | 0.2692 ±0.014 | 0.2751 ±0.012 | 0.2595 ±0.008 | 0.2701 ±0.016 | 0.2651 ±0.017 |
| Tapped bulk density TBD (g/ml) | 0.2973 ±0.025 | 0.3056 ±0.019 | 0.2912 ±0.013 | 0.3123 ±0.011 | 0.3001 ±0.016 |
| Compressibility index (%) | 10.43 | 11.08 | 12.21 | 15.6 | 13.2 |

**Table 4: Pre compression parameter of granules.**

### 3.5. Post compression parameters

The results of physical properties of nicorandil sustained release matrix tablets are presented see Table 5. The thickness of matrix tablets was measured by vernier caliper and was ranged between 3.007±0.001 mm to 3.010±0.002 mm. The diameter of matrix tablets was measured by vernier caliper and was ranged between 6.007±0.002 mm to 6.010±0.001 mm. The hardness of the matrix tablets was measured by Monsanto tester and was controlled between 4.05±0.17 kg/cm$^2$ to 4.39±0.28 kg/cm$^2$. The friability was below 1% for all the formulations. The percentage of drug content for F1 to F5 was found to be in between 99.39±0.43% to 99.96±0.98% of nicorandil, it complies with official specification. Thus all the physical attributes of the prepared tablets were found be practically within control. The nicorandil matrix tablets were off white, smooth, and flat shaped in appearance.

Weight variations for different formulations were found to be 149.88 mg to 150.37 mg. The weight variation is presented, see Table 6.

| Parameters | F1 | F2 | F3 | F4 | F5 |
|---|---|---|---|---|---|
| Thickness (mm) | 3.009±0. 001 | 3.010±0. 002 | 3.007±0. 001 | 3.008±0. 002 | 3.009±0. 002 |
| Diameter (mm) | 6.008±0. 002 | 6.009±0. 001 | 6.009±0. 002 | 6.007±0. 002 | 6.010±0. 001 |
| Hardness (kg/cm²) | 4.32±0.2 1 | 4.05±0.1 7 | 4.39±0.2 8 | 4.09±0.2 8 | 4.26±0.3 7 |
| Friability (%) | 0.284 | 0.391 | 0.358 | 0.273 | 0.304 |
| Drug content (%) | 99.89±0. 37 | 99.39± 0.43 | 99.96±0. 98 | 99.52±0. 26 | 99.83±0. 21 |

**Table 5: Post compression parameter of tablets**

| Sl. No | F-1 | F-2 | F-3 | F-4 | F-5 |
|---|---|---|---|---|---|
| 1 | 150.3 | 150.3 | 150.8 | 149.5 | 149.6 |
| 2 | 150.4 | 150.4 | 150.3 | 149.8 | 149.5 |
| 3 | 150.2 | 151.2 | 149.9 | 149.3 | 149.7 |
| 4 | 150.8 | 151.1 | 149.4 | 150.3 | 149.3 |
| 5 | 149.7 | 150.4 | 149.5 | 151.2 | 148.9 |
| 6 | 149.4 | 150.7 | 149.5 | 150.3 | 150.5 |
| 7 | 150.4 | 150.8 | 149.8 | 150.1 | 152 |
| 8 | 149.2 | 149.1 | 149.6 | 151.7 | 150.3 |
| 9 | 149.2 | 149.4 | 149.1 | 151.9 | 149.4 |
| 10 | 149.7 | 149.7 | 151.3 | 149.6 | 149.6 |
| **Average Weight (mg)** | 149.93 | 150.31 | 149.92 | 150.37 | 149.88 |
| **% Maximum Positive deviation** | 0.31 | 0.6 | 0.92 | 1.02 | 1.41 |
| **% Minimum Negative deviation** | 0.49 | 0.81 | 0.35 | 0.71 | 0.65 |

**Table 6: Weight variation of tablets.**

### 3.6 *In-vitro* dissolution studies

The cumulative percentage drug release for F-1, F-2, F-3, F-4 and F-5 was (97.8%, 96.5%, 96.8%, 90.7% and 86.5%) at the end of 12 h respectively. Formulation F1 and F2 failed to sustain release beyond 11 h. Among all the formulations, F3 showed 96.8% release at the end of 12 h. It was found cumulative percentage of drug release decreases with increase in the mangifera gum concentration. The in-vitro release of the formulation is presented, see Figure 1.

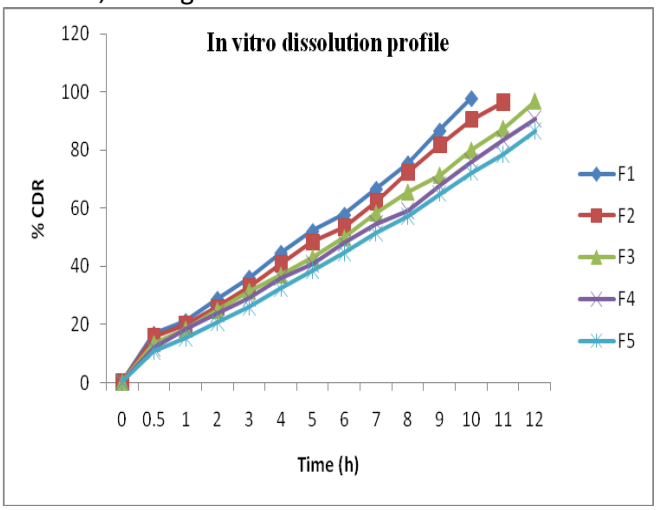


**Figure 1: *In-vitro* dissolution profile of sustained release tablets**



 

### 3.7. Drug release kinetics

The release data was fitted to various mathematical models to evaluate the kinetics and mechanism of the drug release, see Table 7. The regression coefficient obtained for zero order kinetics were found to be higher ($R^2$:0.992 to 0.997) when compared with those of the first order kinetics ($R^2$: 0.726 to 0.910), indicating that drug release from all the formulations followed zero order kinetics. In this experiment, the in-vitro release profiles of drug from all these formulation could be best expressed by Higuchi's equation as the plots showed the highest linearity ($R^2$: 0.992 to 0.997). To confirm the diffusion mechanism the data was fitted into Korsemeyer-Peppas equation. All the formulation showed good linearity ($R^2$:0.953 to 0.970) with slope (n) values ranging from 0.592 to 0.662. The mechanism of release from formulation F1 to F5 showed behaviors of anomalous (non-Fickian) diffusion. The n values increases as the drug gum ratio of the tablet increases. This n value appears to indicate a coupling of diffusion and erosion mechanism (known anomalous non-Fickian diffusion). Hence, diffusion coupled with erosion might be mechanism for the drug release from mangifera gum sustained release based matrix tablets.

| Formulations | Zero order plots¤ | First order plots▪ | Higuchi's plots● | Korsmeyer et al's plots□ | |
|---|---|---|---|---|---|
| | | | | Slope(n) | $R^2$ |
| F1 | 0.992 | 0.726 | 0.992 | 0.592 | 0.970 |
| F2 | 0.993 | 0.817 | 0.993 | 0.608 | 0.970 |
| F3 | 0.996 | 0.803 | 0.996 | 0.626 | 0.958 |
| F4 | 0.995 | 0.881 | 0.995 | 0.627 | 0.951 |
| F5 | 0.997 | 0.910 | 0.997 | 0.662 | 0.953 |

¤Zero order equation, C=K0 t. ▪First order equation, LogC=logC□-Kt/2.303.
●Higuchi's equation, Q= Kt½. □Korsmeyer et al's equation, Mt/Mα= Ktn.

**Table 7: Release kinetics parameters of designed sustained release matrix tablets of Nicorandil**

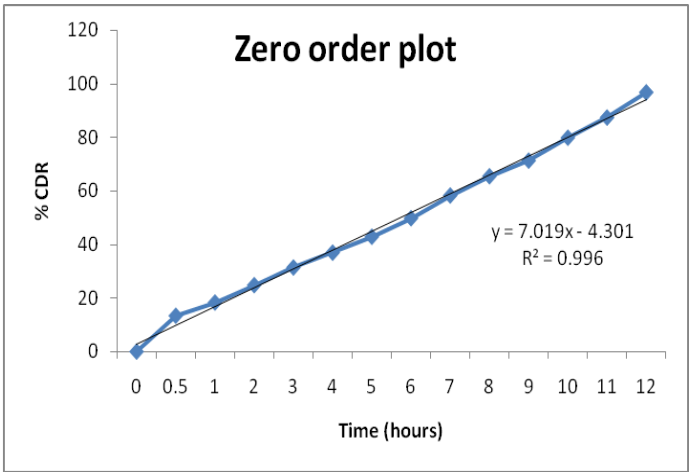


**Figure 2: Zero order release kinetics of optimized formulation F3**

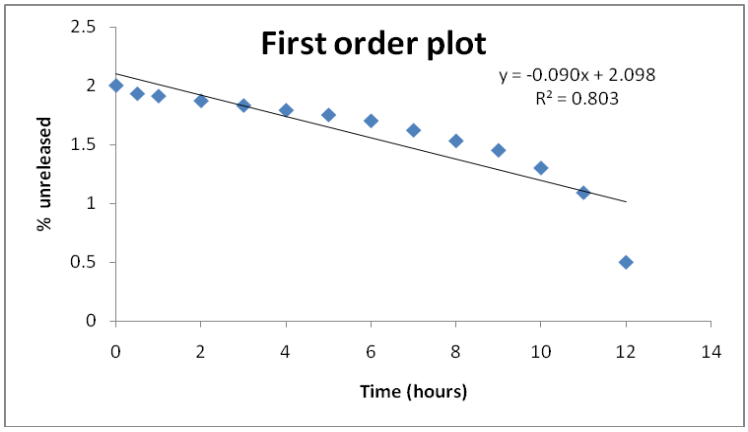


**Figure 3: First order release kinetics of optimized formulation F3**

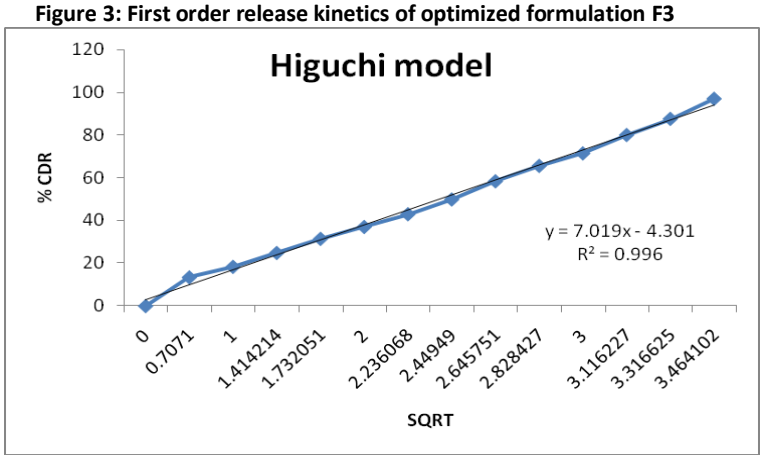


**Figure 4: Higuchi model release kinetics of optimized formulation F3**

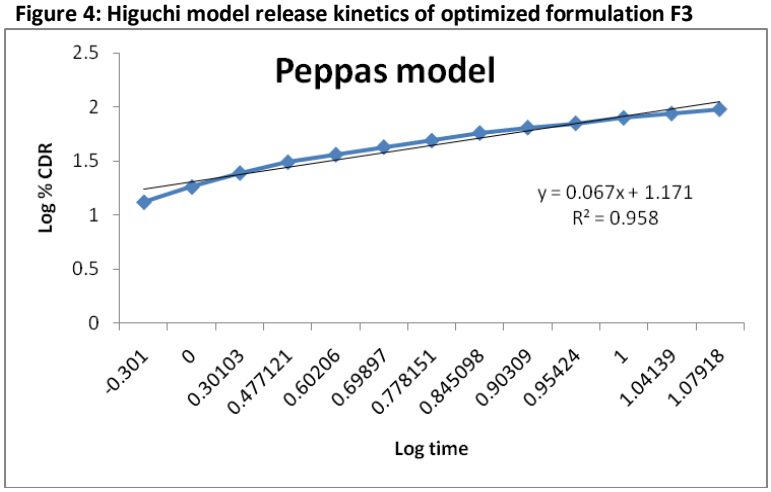


**Figure 5: Korsmeyer and Peppas release kinetics of optimized formulation F3**

### 3.8. Stability study

The optimized formulation F3 was kept at accelerated (40±2°C/75±5% RH) storage conditions for a period of 3 months. After stability test period, tablets were analyzed for drug content, hardness, friability and in-vitro release. Stability studies result showed that there was no significant change in hardness, friability, drug content, and dissolution profile of formulation F3. The formulation was stable under accelerated condition.

### 4. CONCLUSION

From the above observations it is concluded that slow and sustained release of nicorandil over a period of 12 h was obtained from matrix tablets (F1 to F5). Use of natural



 

gum *Mangifera indica* was successful in the formation of matrix tablets and at the same time it is effective in retarding the drug release. Among all the formulation, F3 shows that 96.8% of drug release at the end of 12 h. The cumulative percentage drug release was decreased by increase in mangifera gum concentration. The stability studies show that there was no significant change in hardness, friability, and drug content of optimized formulation F3. Diffusion coupled with erosion might be the mechanism for the drug release from mangifera gum based matrix tablets which can be expected to reduce the frequency of administration and decrease the dose-dependent side effects associated with repeated administration of conventional nicorandil tablets.

## 5. ACKNOWLEDGEMENT

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