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# Design, Formulation and Evaluation of Drug Loaded Nanoparticles of Naproxen by Using Eudragit Rs-100

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**KEYWORDS**
Naproxen, Polymethyal Metha crylate, Eudrgit Rs 100, Drug entrapment efficiency

**ABSTRACT**:
In this research work we formulated biodegradable polymethyl metha crylate and eudragit RS-100 nanoparticles (NPs) containing Naproxen by nano-precipitation solvent displacement method to achieve a better free release profile for intra articular injection with improved efficacy. Dissolution study was revealed that increase the release of Naproxen from NPs. The particle size and size distribution of the Naproxen loaded PMMA and Eudragit Rs 100 nanoparticles were characterized by using a Zetasizer. The *in vitro* drug release indicated that the formulation NA2, NA4, NA5 And NA7 were not suitable for anti-inflammatory agent of drug as maximum amount of drug was released in the physiological environment of stomach and small intestine within 5 hours. Whereas, NA1, NA3 and NA6 formulations have released small amount of drug within 5 hours and 81.16%, 78.12% and 82.54% of drug was targeted to anti- inflammatory region from NA1,NA3and NA7. The results indicated that the prepared formulation was intact upto 12hrs. and transit was clearly seen. Drug release mechanism followed Non-Fickian transport.

**Introduction**
Arthritis commonly known as degenerative joint inflammation of different types of joints, causes severe ache & rigidness that can worsen through the age Signsen compass pain, swelling, lowered varies of movement and hardness. Arthritis of two types;

- Osteoarthritis(OA)
- Rheumatoid arthritis(RA)

**Treatment:**
There isn't any deal with for arthritis, but there are a lot of therapies are to lend a hand relieve the ache and in capacity that it may reason for disease. Over-the-counter medicines will probably be used to keep an eye on ache and irritation with joints in human body. These medicines are referred to as anti-inflammatory drugs. Include in aspirin, ibuprofen and naproxen and some of drugs. Paracetamol can be useful in controlling ache and now and again relieve pain. Injections of cortisone into the joint may also for the time being assist to relieve ache and swelling in the body. Viscos supplementation or injection of hyaluronic acid preparations can additionally be beneficial in lubricating the joint. This is often carried out in the knee. In frequently an orthopedic healthcare professional will function surgical procedure for arthritis when different strategies of nonsurgical

Journal of Chemical Health Risks

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remedy have unsuccessful to relieve ache and different symptoms. [1]

**NANOPARTICLES:**

Nanotechnology employs data from the fields of physics; chemistry, biology, substances science, fitness sciences and engineering. It has large functions in nearly all the fields of science and fitness sciences. Nanoparticles can be referred to as particulate dispersions or strong particles with a dimension in the vary of 10-1000 nm[2]**.** Nanoparticles are the spherical amorphous particles which bind, absorb, and transmit the drug to the targeted of site. Pharmaceutical nanotechnology makes a specialty of formulating therapeutically vs brokers in biocompatible nano forms a into nanoparticles, nanocapsules, micellar systems, and conjugates. These programs supply numerous benefits in drug delivery, mostly specializing in doubled safety and efficacy of the drugs. e.g. offering centered free up of medicine recovering bioavailability extending impact in targeted for tissue and cell, and convalescing the steadiness of therapeutic brokers towards chemical/enzymatic degradation these nanoparticles are the matrices where the drug is entrapped and encapsulated insideit.[3-6]

**MATERIALS AND METHOD**

From Sahydri chemicals Pvt Ltd Mumbai, Naproxen was purchased. From HiMedia Laboratories Pvt. Ltd. Polvinyl alcohol, Polymethyl methacrylate were received.

**Estimation of Naproxen:**

Spectrophotometric strategy dependent on the estimation at 232 nm of UV Region in 0.1 NHCL of pH 1.2 and phosphate cushion of pH 7.4 was utilized for the estimation of mefenamic corrosive.

**Preparation of standard curve of Naproxen in PH1.2 (0.1NHCL) &pH 7.4**

100 mg of Naproxen had been effectively weighed and dissolve in 100 ml ethanol used in a 100 ml volumetric flask. This is primary inventory solution containing 1000 µg/ml. From this number one stock solution, 1ml was pipette out and transferred in to a 100 ml neither volumetric flask and volume changed into made as much as 100 ml with 0.1 N HCL & separately another in pH 7.4 which contained the attention of 10µg/ml. From second stock solution aliquots corresponding to 1-5µg/ml (1, 2, 3, 4 5 ,6 ml) were pipette out into a sequence of 10 ml volumetric flask and volume where made up to 10ml with 0.1 N HCL. The absorbance of these solutions was calculated at 232 nm by using UV-visible double beam spectrophotometer.[7]

**Preparation of Naproxen Nanoparticles**

**Solvent displacement method**:

The preparation of PMMA nanoparticles was prepared by using Nano precipitation-solvent displacement method. Accurately weighed PMMA is dissolved in acetone by invariable stirring and at 60˚C. Naproxen was weighed accurately and dissolved in it. The organic solution like ethanol or methanol and dichloromethane, was poured drop wise into an aqueous solution, at 1ml/ min through the nozzle into the preservative containing 60 ml distilled water, which was stirred at 1500 rpm for 2hrs. The organic solvent was evaporated under in the room temperature (35˚C) to form colloidal suspension. Formulation of naproxen nanoparticles was shown in table 1. Nanoparticles were removed by centrifugation and supernatants were discarded.[8]

**Table 1.** Formulation details of Naproxen nanoparticles

| Ingredient (mg) | NP01 | NP02 | NP03 | NP04 | NP05 | NP06 | NP07 |
|---|---|---|---|---|---|---|---|
| DRUG | 200 | 200 | 200 | 200 | 200 | 200 | 300 |
| EU RS100 | 400 | 600 | 800 | - | - | - | 500 |
| PMMA | - | - | - | 400 | 600 | 800 | 500 |
| PVA | 600 | 600 | 600 | 600 | 600 | 600 | 600 |
| DCM(ml) | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| WATER (ml) | 100 | 100 | 100 | 100 | 100 | 100 | 100 |

**RESULTS AND DISCUSION**

**Table 2.**Spectrophotometric data for the estimation of Naproxen in 0.1 HCL

| Sr. No. | Concentration (mcg/ml) | Absorbance |
|---|---|---|
| 1 | 0 | 0 |
| 2 | 1 | 0.016 |
| 3 | 2 | 0.056 |
| 4 | 3 | 0.064 |
| 5 | 4 | 0.086 |

Journal of Chemical Health Risks
www.jchr.org
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| | | |
|---|---|---|
| 6 | 5 | 0.104 |
| 7 | 6 | 0.116 |

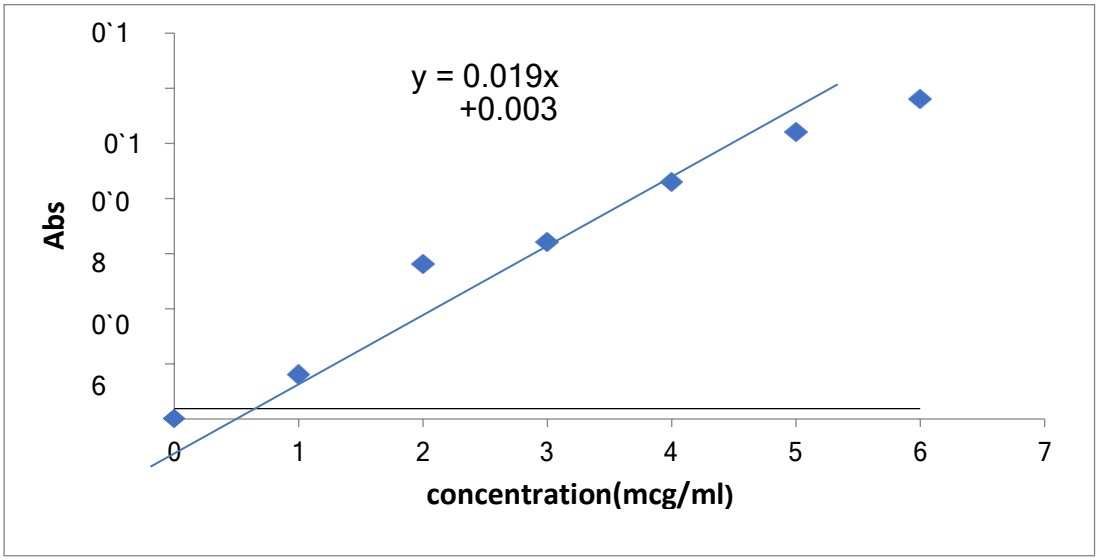


**Figure 1.** Calibration curve for the estimation of Naproxen in 0.1 N HCl

**Table 3.** Spectrophotometric data for estimation of Naproxen in phosphate buffer pH 7.4

| Sr. No. | Concentration (mcg/ml) | Absorbance |
|---|---|---|
| 1 | 0 | 0 |
| 2 | 1 | 0.015 |
| 3 | 2 | 0.123 |
| 4 | 3 | 0.211 |
| 5 | 4 | 0.242 |
| 6 | 5 | 0.301 |
| 7 | 6 | 0.316 |

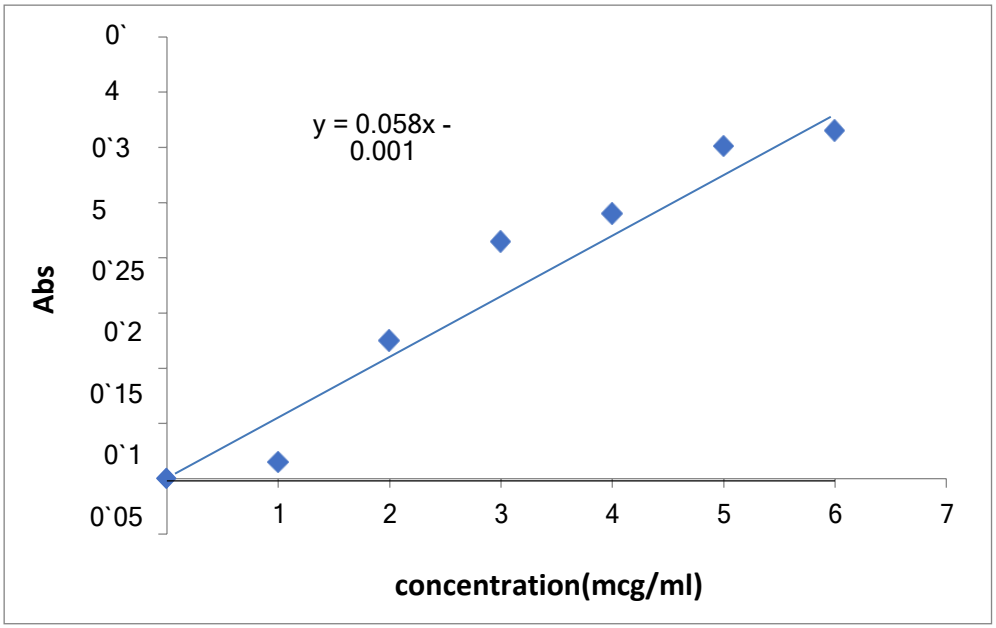


**Figure 2.** Calibration curve for Naproxen in phosphate buffer pH 7.4

Journal of Chemical Health Risks

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JCHR (2023) 13(4s), 206-213 | ISSN:2251-6727

The drug Naproxen was scanned between 200-400 nm in both 0.1 N HCl & phosphate buffer pH 7.4 and a $\lambda_{max}$ of 232 was selected for further studies. The calibration curve for Naproxen was performed in 0.1 N HCl of pH 1.2, phosphate buffer and phosphate buffer of pH7.4. The Beer's law was obeyed in the range of 1 to 6 mcg/ml. The $r^2$ values were 0.974, and 0.951; slope values were 0.019 and 0.058 and intercept values were 0.003 and 0.001 respectively for 0.1 N HCl, phosphate buffer pH 7.4. The high $r^2$ values suggest that there is linearity between drug concentration and corresponding absorbance. Further, calculations of entrapment efficiency and drug release are based on the data of these calibration curves.

**Table 5.** Measurement of Particle size, zeta potential and drug entrapment efficiency (DEE) for prednisolone nanoparticles

| Formulation Batches | Particle Size (nm) | Zeta Potential (mV) | DEE(%) |
|---|---|---|---|
| NP1 | 256.4 | -34.65 | 39.17± 0.85 |
| NP2 | 304.3 | -36.25 | 48.25± 0.74 |
| NP3 | 343.8 | -40.35 | 59.45± 1.54 |
| NP4 | 386.4 | -44.56 | 65.25± 0.48 |
| NP5 | 426.1 | -35.15 | 62.38± 0.59 |
| NP6 | 451.6 | -42.37 | 68.54± 0.44 |
| NP7 | 480.2 | -45.14 | 75.14± 0.19 |

**All the values average of three determinations ± indicates SD values**

**Table 6.** *In vitro* drug release data of Naproxen from NA1, NA2, NA3 nanoparticles

| Sr. No. | Time (hrs) | Square root of time (hrs) | Log Time (hrs) | NA1 | | NA2 | | NA3 | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | % drug released | Log % drug released | % drug released | Log % drug released | % drug released | Log % drug released |
| 1 | 0.0 | 0.000 | 0.000 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 0.5 | 0.707 | 0.301 | 6.74 | 0.82 | 8.12 | 0.90 | 7.61 | 0.88 |
| 3 | 1 | 1.000 | 0.000 | 13.81 | 1.14 | 15.63 | 1.19 | 14.06 | 1.14 |
| 4 | 1.5 | 1.225 | 0.176 | 18.72 | 1.27 | 21.41 | 1.33 | 20.40 | 1.30 |
| 5 | 2 | 1.414 | 0.301 | 24.58 | 1.39 | 26.24 | 1.41 | 27.72 | 1.44 |
| 6 | 3 | 1.732 | 0.477 | 30.29 | 1.48 | 32.74 | 1.51 | 33.76 | 1.52 |
| 7 | 4 | 2.000 | 0.602 | 37.67 | 1.52 | 38.81 | 1.58 | 40.21 | 1.60 |
| 8 | 5 | 2.236 | 0.698 | 41.48 | 1.61 | 46.10 | 1.66 | 44.54 | 1.64 |
| 9 | 6 | 2.449 | 0.778 | 47.04 | 1.67 | 52.29 | 1.71 | 48.12 | 1.68 |
| 10 | 7 | 2.646 | 0.845 | 53.18 | 1.72 | 58.34 | 1.76 | 52.18 | 1.71 |
| 11 | 8 | 2.828 | 0.903 | 60.72 | 1.78 | 62.31 | 1.79 | 59.34 | 1.77 |
| 12 | 9 | 3.102 | 1.000 | 65.58 | 1.81 | 68.08 | 1.83 | 63.76 | 1.80 |
| 13 | 10 | 3.464 | 1.079 | 71.32 | 1.85 | 73.81 | 1.86 | 69.51 | 1.84 |
| 14 | 11 | 3.316 | 1.041 | 76.23 | 1.88 | 78.19 | 1.89 | 74.09 | 1.86 |
| 15 | 12 | 3.464 | 1.079 | 81.16 | 1.90 | 84.06 | 1.92 | 78.12 | 1.89 |

**Table 7.** *In vitro* release data of Naproxen fromNA4,NA5,NA6,NA7 nanoparticles

| Sr. No. | Time (hrs) | Square root of time (hrs) | Log Time (hrs) | NA4 | | NA5 | | NA6 | | NA7 | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | % drug released | Log %drug released | % Drug released | Log % drug released | % Drug released | Log % drug Released | % Drug released | Log %drug released |
| 1 | 0.0 | 0.000 | 0.000 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 0.5 | 0.707 | 0.301 | 9.51 | 0.97 | 8.14 | 0.91 | 5.74 | 0.77 | 13.62 | 1.13 |
| 3 | 1 | 1.000 | 0.000 | 16.19 | 1.20 | 17.74 | 1.24 | 11.87 | 1.07 | 19.26 | 1.28 |
| 4 | 1.5 | 1.225 | 0.176 | 21.41 | 1.33 | 25.64 | 1.40 | 17.41 | 1.24 | 27.56 | 1.44 |
| 5 | 2 | 1.414 | 0.301 | 28.86 | 1.46 | 31.51 | 1.49 | 22.36 | 1.34 | 32.38 | 1.51 |
| 6 | 3 | 1.732 | 0.477 | 36.47 | 1.56 | 39.48 | 1.59 | 28.12 | 1.44 | 39.73 | 1.59 |
| 7 | 4 | 2.000 | 0.602 | 42.76 | 1.63 | 44.06 | 1.64 | 33.19 | 1.52 | 45.54 | 1.65 |
| 8 | 5 | 2.236 | 0.698 | 50.31 | 1.70 | 52.21 | 1.71 | 40.59 | 1.60 | 51.12 | 1.70 |
| 9 | 6 | 2.449 | 0.778 | 56.22 | 1.74 | 57.84 | 1.76 | 46.28 | 1.66 | 58.21 | 1.76 |
| 10 | 7 | 2.646 | 0.845 | 61.18 | 1.78 | 63.71 | 1.80 | 52.44 | 1.71 | 62.08 | 1.79 |

Journal of Chemical Health Risks

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JCHR (2023) 13(4s), 206-213 | ISSN:2251-6727

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|---|---|---|---|---|---|---|---|---|---|---|---|
| 11 | 8 | 2.828 | 0.903 | 66.23 | 1.80 | 69.12 | 1.83 | 59.08 | 1.77 | 68.38 | 1.83 |
| 12 | 9 | 3.102 | 1.000 | 70.17 | 1.84 | 74.08 | 1.86 | 65.10 | 1.81 | 73.22 | 1.86 |
| 13 | 10 | 3.464 | 1.079 | 76.38 | 1.88 | 79.16 | 1.89 | 71.51 | 1.85 | 79.17 | 1.89 |
| 14 | 11 | 3.316 | 1.041 | 81.43 | 1.91 | 84.21 | 1.92 | 76.06 | 1.88 | 87.68 | 1.94 |
| 15 | 12 | 3.464 | 1.079 | 87.12 | 1.94 | 89.29 | 1.95 | 82.54 | 1.91 | 92.78 | 1.96 |

Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(4s), 206-213 | ISSN:2251-6727

**Table 8.** Kinetic values of Naproxen release from nanoparticles

| Nanoparticles | Zero order | | First order | |
|---|---|---|---|---|
| | ***N*** | ***R*** | ***N*** | ***R*** |
| NA1 | -16.08 | 0.998 | 0.915 | 0.650 |
| NA2 | -14.85 | 0.997 | 0.963 | 0.620 |
| NA3 | -12.63 | 0.993 | 0.956 | 0.608 |
| NA4 | -14.20 | 0.993 | 0.997 | 0.601 |
| NA5 | -13.68 | 0.991 | 1.013 | 0.585 |
| NA6 | -18.48 | 0.999 | 0.875 | 0.681 |
| NA7 | -12.14 | 0.993 | 1.066 | 0.556 |

**Table 9.** Kinetic values of Naproxen release from nanoparticles

| Nanoparticles | Higuchi Equation | | Korsemeyer's Equation | |
|---|---|---|---|---|
| | ***N*** | ***R*** | ***N*** | ***R*** |
| NA1 | 16.18 | 0.998 | 0.133 | 0.933 |
| NA2 | 14.85 | 0.997 | 0.633 | 0.700 |
| NA3 | 12.63 | 0.993 | 0.726 | 0.700 |
| NA4 | 14.20 | 0.993 | 0.853 | 0.675 |
| NA5 | 13.68 | 0.991 | 0.874 | 0.648 |
| NA6 | 18.48 | 0.999 | 0.733 | 0.736 |
| NA7 | 12.14 | 0.993 | 0.929 | 0.629 |

**R:Corelation Coefficients, N:Release Mechanism**

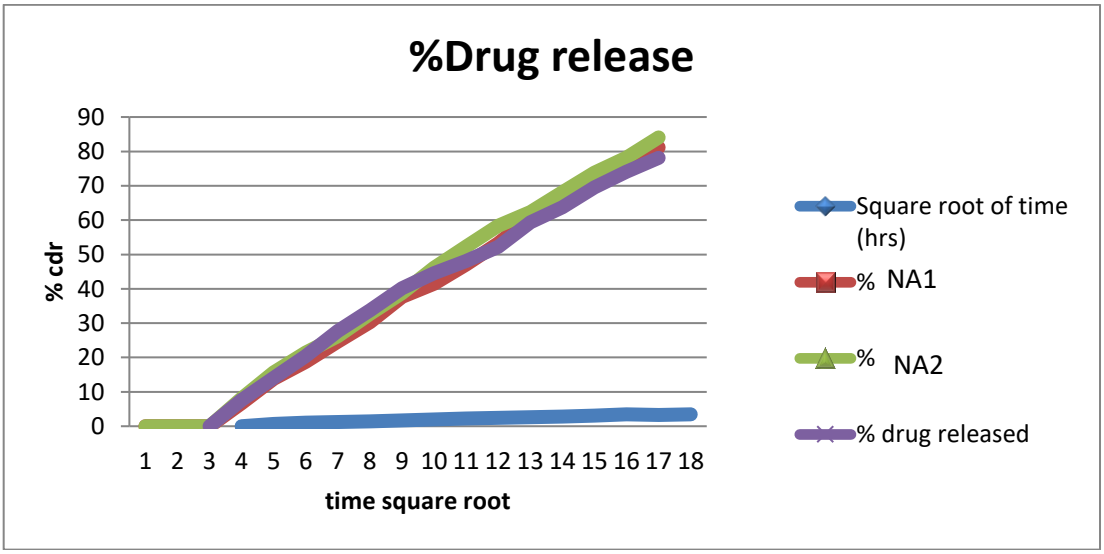


**Figure 3.** % Drug release VS Square root of time of formulations NA1 & NA2

Journal of Chemical Health Risks

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JCHR (2023) 13(4s), 206-213 | ISSN:2251-6727

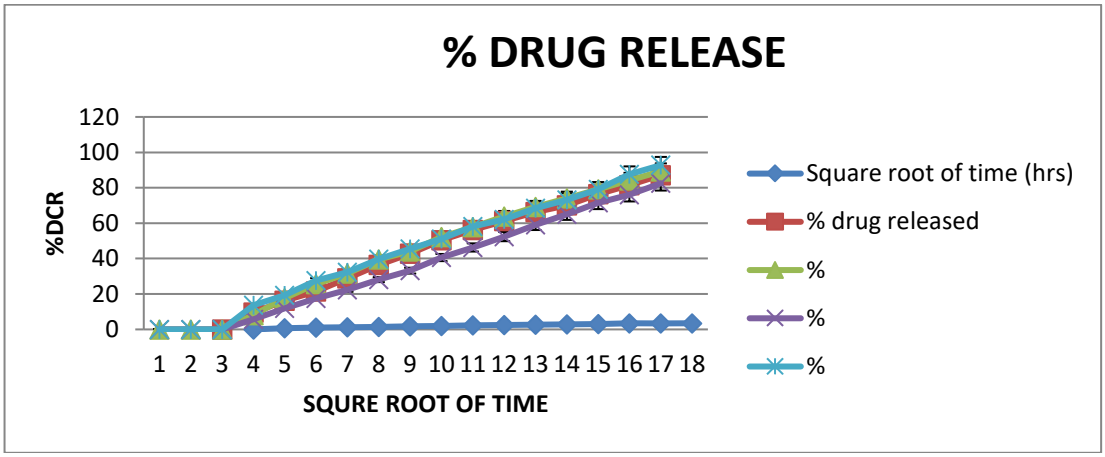


**Figure 4.** % Drug release VS Square root of time of formulations

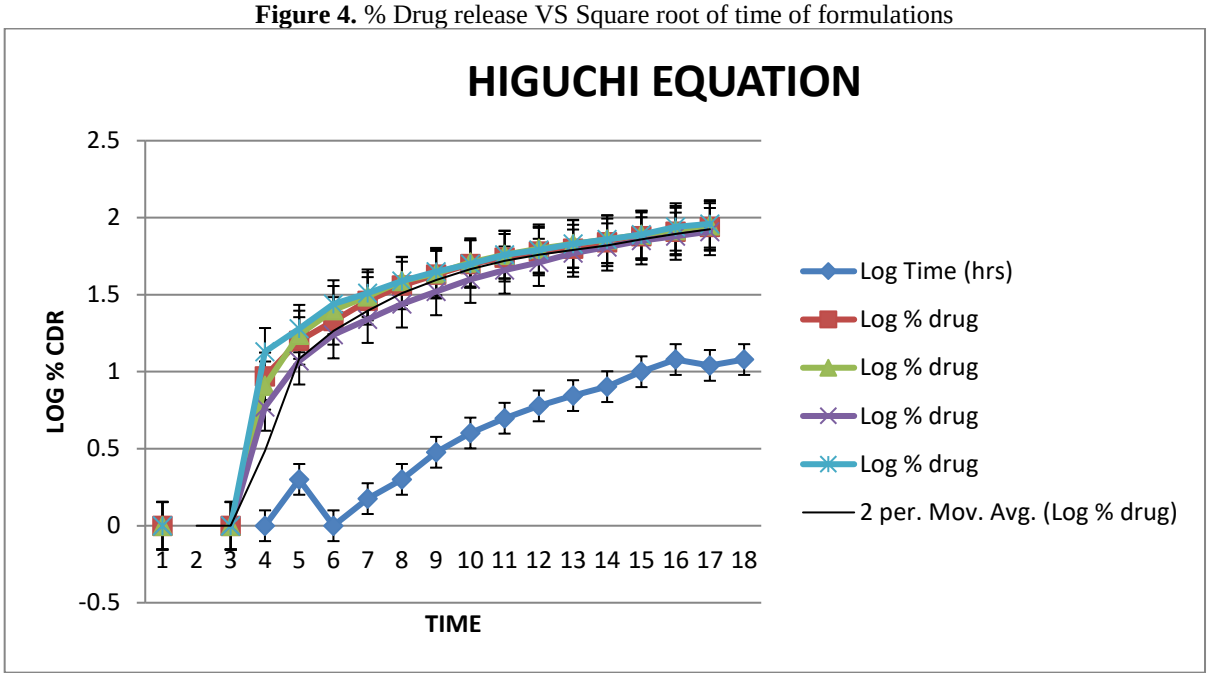


**Figure 5.** Higuchi plots

**DISCUSSION**

We have developed polymeric nanoparticles using polymethyl methacrylate by solvent displacement method for the sustained release of Naproxen. The size of nanoparticles is along zeta potential is recorded in Table 5. The average size of nanoparticles was found to be in the range of 256.4 to 480.2 nm. With increasing the concentration of polymer, we observed an increase in size of the nanoparticles. However, by increasing the amount of Naproxen also, the size was increased. The drug entrapment efficiency (DEE) of the nanoparticles was carried by soaking method and the results are summarized in Table 5. The DEE was found to be in the range of 39.19% to 75.14%. As the concentration of polymer was increased in the nanoparticles, the DEE was decreased. But an increase in amount of Naproxen resulted in increased DEE.

The *in-vitro* drug release study was performed by using dialysis method in 0.1 N HCl (pH 1.2) and phosphate buffer (pH7.4). The dissolution profiles of Naproxen are given in Figure 3 & 4 and data are presented in Tables 6 & 7. 81.16, 84.06, 78.12, 87.12, 89.29, 82.54, and 92.78 % Naproxen was released from NA1, NA2, NA3, NA4, NA5, NA6, and NA7 formulations respectively at the end of 12 hour. These results suggested that as the concentration of polymer was increased, the drug release rate was decreased and on the other hand, as well as the amount of Naproxen was increased the drug release was increased. We also noticed that as concentration of PVA was increased there was a little decrease in drug release. The drug release was continued upto 12 hours depending upon the formulation variables.

The release data were fitted according to Higuchi's

Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(4s), 206-213 | ISSN:2251-6727

equation and Korsemeyer's equation and the mechanism of drug release was calculated according to Peppas equation. The calculated *n* values along with the correlation coefficients have been shown in Table 8 & 9. The values of *n* depend upon the polymer concentration; the *n* values increase with increase in polymer concentration and suggest that the mechanism of drug release followed non-Fickian transport mechanism. The release data was equipped according to Zero order equation and first order equation are the mechanism of drug release where calculated according to zero order equation. The calculated *n* values along with the correlation coefficients have been shows in Table 8 & 9. The value of *n* depends upon the polymer concentration.

## CONCLUSION

In this research work we had developed polymethyl methanacrylate nanoparticles loaded with Naproxen for improved treatment of anti-arthritics agent. The nanoparticles were characterized by particles size, zeta potential, entrapment efficiency. Then *in- vitro* drug release activity was also performed. This prepared nanoparticles were spherical with some looser aggregates. The *in vitro* drug release indicated that the formulation NA2, NA4, NA5 And NA7 were not suitable for anti-inflammatory agent of drug as maximum amount of drug was released in the physiological environment of stomach and small intestine within 5 hours. Whereas, NA1, NA3 and NA6 formulations have released small amount of drug within 5 hours and 81.16%, 78.12%and 82.54% of drug was targeted to anti- inflammatory region from NA1,NA3and NA7. The results indicated that the prepared formulation was intact upto 12hrs. and transit was clearly seen. The drug release mechanism followed by non-Fickian transport.

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