RESEARCH ARTICLE

Drug Release Kinetics and Comparative Study of Oxaprozin Nonogel with Market Formulation

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ABSTRACT
The proposed work was aimed to Drug release kinetics and comparative studies of a nanotechnology-based formulation of oxaprozin nanogel. In this prepared and optimized formulation of F-7 nanogel formulation performed the drug release kinetic studies with model dependent strategies depend on various numerical functions, which depict the release profile. When an appropriate capacity has been chosen, the release profiles are assessed relying upon the determined model boundaries. The information acquired from ex vivo permeation studies were plotted in various models of data treatment and compared with market formulation Ibugic gel manufactured by Cipla pharmaceutical Ltd. Data observed as drug release kinetics studies in each situation, R^2 value was determined from the chart and detailed. Zero order release kinetics was found (R^2=0.992) to fit the release data best and the % drug release for optimized up to 17 hours of F-7 formulation was found 95.89% which was higher than the market formulation nanogel 92.31% up to same time duration 17 hours.
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INTRODUCTION

Osteoarthritis commonly affects the hands, feet, spine, and the large weight-bearing joints, such as the hips and knees, although in theory, any joint in the body can be affected. As osteoarthritis progresses, movement patterns (such as gait), are typically affected.[1] Osteoarthritis is the most common cause of a joint effusion of the knee.[2] In smaller joints, such as those in the fingers, hard bony enlargements—referred to as Heberden's nodes (on the distal interphalangeal joints) or Bouchard's nodes (on the proximal interphalangeal joints) may form. While these nodes are not necessarily painful, they can significantly limit finger movement. Additionally, osteoarthritis in the toes may contribute to the development of bunions,[3] causing redness and swelling.

The significant limitation of drug administration via the intra-articular route has been a major focus in research. It is estimated that the half-life in the joint fluid of small drug molecules, e.g. NSAIDs and large polymeric molecules, e.g. hyaluronic acid and recombinant proteins, is low (several hours). In recent decades, an extensive literature has demonstrated that nanotechnology approach can result especially attractive as drug delivery carriers for the effective management of OA [4-6].

The drug release from a drug delivery system (DDS) encompasses both dissolution and diffusion mechanisms. numerical equations models depict drug dissolution and/or release from DDS. In the modern era of controlled-release oral formulations, 'Higuchi equation' has become a prominent kinetic equation in its own right, as proven by utilizing drug dissolution studies that are recognized as a significant component in drug delivery advancement [5-9]. Today the Higuchi equation is viewed as one of the widely used and the most well-known controlled-release equation.

MATERIALS AND METHODS

Preparation of Oxaprozin Nanogel

An accurately weighed amount of the drug, Eudragit S-100 (polymer), and Tween-80 (stabilizer) are dissolved in glycerol under continuous stirring. Prepared aqueous phase containing Carbopol-940 dissolved in water with continuous stirring and heat. The drug phase, sonicated using an ultrasonic bath sonicator, is gradually added drop by drop into the aqueous phase during the homogenization process to create the emulsion. The emulsion converted into nanodroplets by homogenizer which formed O/W emulsion [10-12]. Homogenization was continued for one hour. Triethanolamine was incorporated into the mixture while stirring continuously to form the nanogel.

Batch -A formulation F1, F2, F3 was prepared at highest rpm 8000 with variation in composition. Whereas prototype Batches-B formulation F4, F5, F6 and Batch-C formulation F7, F8, F9 prepared at different rpm 5000, 6000, 7000 using homogenizer respectively. The optimized formulation according to data observed the F-7. This nanogel formulation was further studies for drug release kinetic studies and comparative study with market formulation.

Drug release kinetics

Model dependent strategies depend on various numerical functions, which depict the release profile. When an

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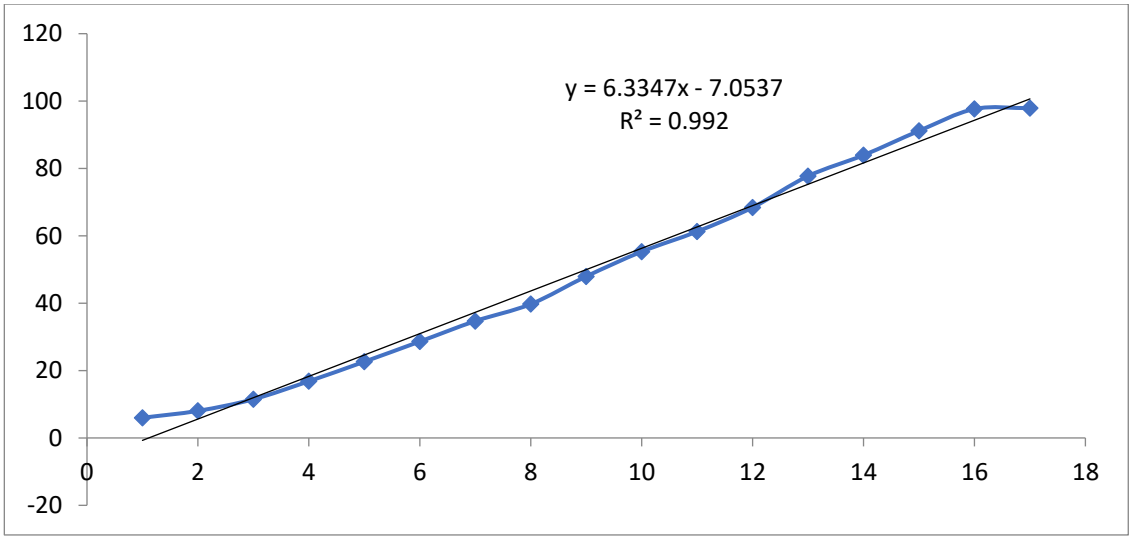


Figure 1: Zero order release kinetics of optimized F-7 formulation

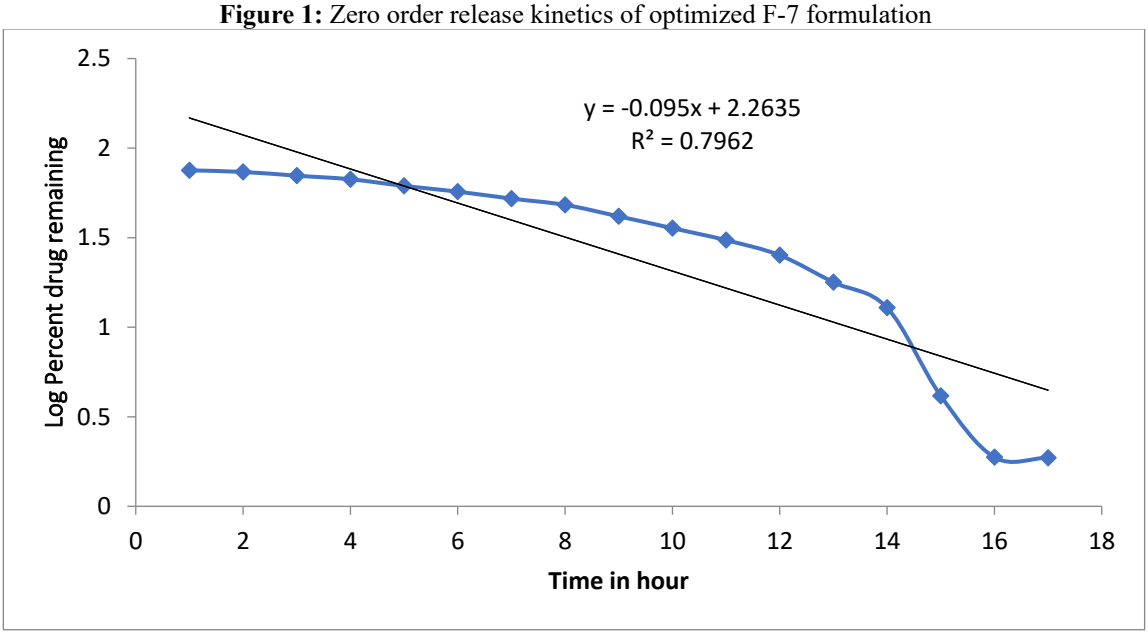


Figure 2: First order release kinetics of optimized F-7 formulation

appropriate capacity has been chosen, the release profiles are assessed relying upon the determined model boundaries. The information acquired from ex vivo permeation studies were plotted in various models of data treatment as follows;

Zero order kinetics

It can be utilized to portray the drug dissolution of few kinds of modified delivery pharmaceutical dosage forms, as an account of some transdermal system, as well as matrix tablets with low soluble drugs in covered structures, osmotic systems, etc. In its least complex structure, zero order release can be represented as:

Q0 - Qt = K0t

Where Qt represents the amount of drug dissolved at time t, Q0 is the initial amount of drug in the solution (often Q0 = 0), and K0 is the zero-order release constant, expressed in units of concentration/time [13]. To analyze the release kinetics, data from in vitro drug release studies were plotted as the cumulative amount of drug released versus time.

First order kinetics

It can be utilized to describe the drug dissolution in pharmaceutical dosage forms for example those containing water- dissolvable drugs in permeable networks. The release of a drug that follows first-order kinetics is represented by the equation:

$$\log C = \log C_0 - \frac{K.t}{2.303}$$

Where,

C0 is the initial drug concentration

k is the first order rate constant

C is Cumulative amount of drug release with time t

t is the time.

When the data is plotted as the logarithm of the cumulative percentage of drug remaining versus time, the result is a straight line with a slope of K/2.303.

Higuchi's Model

The release of a drug from a drug delivery system (DDS) involves both the processes of dissolution and diffusion. Several numerical equations models depict drug dissolution and/or release from DDS. In the modern era of controlled-release oral formulations, 'Higuchi equation' has become a

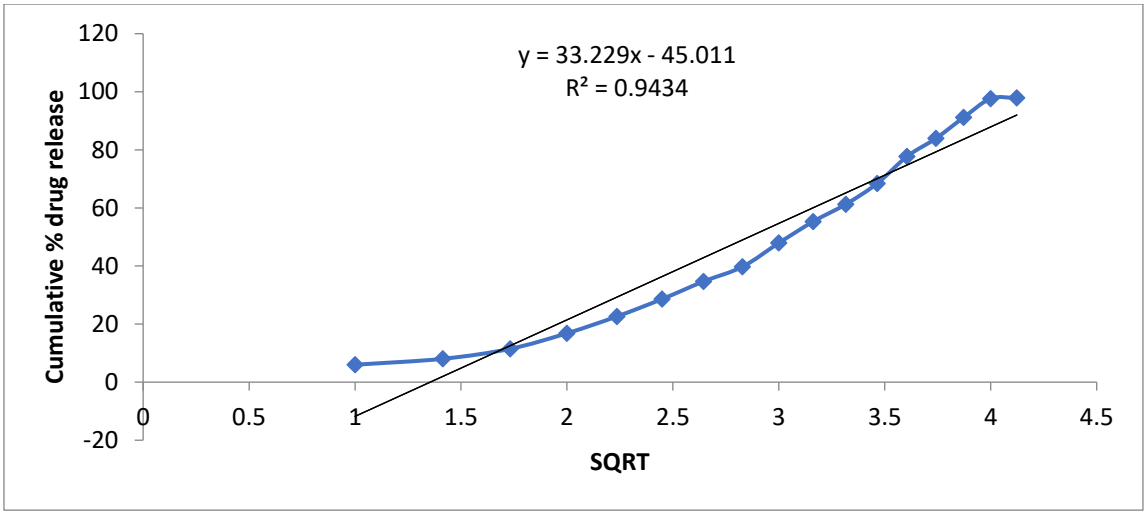


Figure 3: Higuchi's Model release kinetics of optimized F-7 formulation

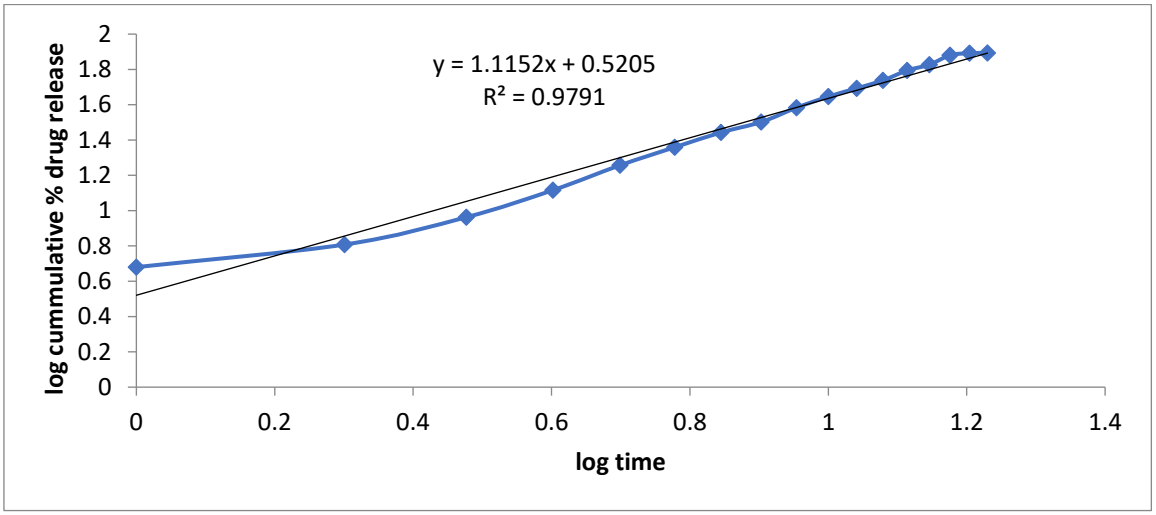


Figure 4: Korsmeyer-peppas release kinetics of optimized F-7 formulation

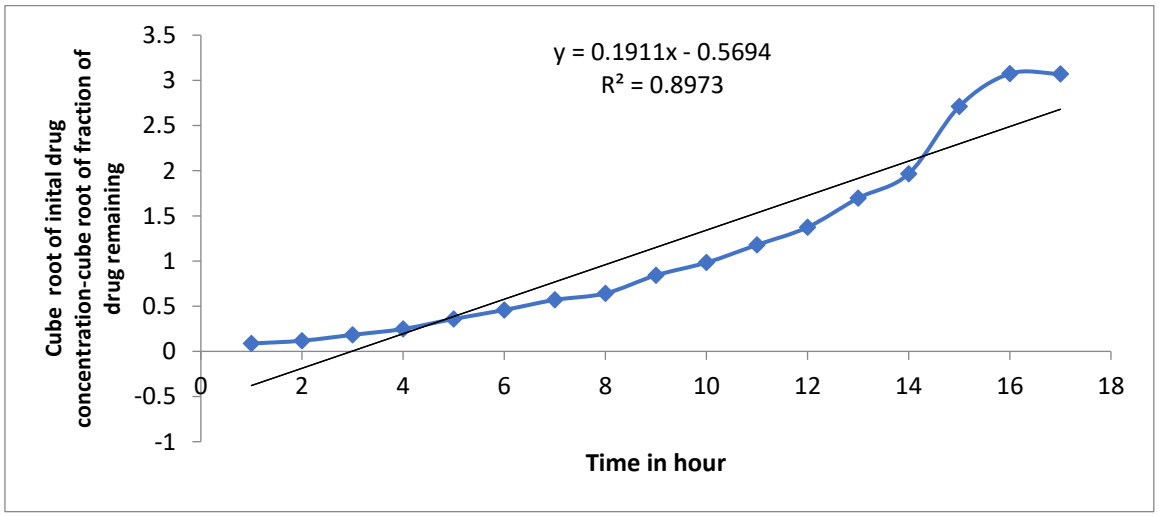


Figure 5: Hixson Crowell release kinetics of optimized F-7 formulation

prominent kinetic equation in its own right, as proven by utilizing drug dissolution studies that are recognized as a significant component in drug delivery advancement. Today the Higuchi equation is viewed as one of the widely used and the most well-known controlled-release equation [14]. The classical basic Higuchi This model is based on the hypotheses that

- Initial drug concentration in the tablet is a lot higher than drug dissolvability.
-Drug diffusion happens just in one measurement (edge impact should be irrelevant).

Table 1: Kinetic equation parameter of formulation F-7

Formulation	Zero order		First order		Higuchi		Peppas		Hixson	
	R^2	K_0	R^2	K_0	R^2	K_0	R^2	K_0	R^2	K_0
F-7	0.992	6.334	0.7962	0.095	0.9434	33.229	0.9791	1.1152	0.897	0.1911

- The drug particles are significantly smaller than the thickness of the system.
- Matrix swelling and dissolution are irrelevant.
- Drug diffusivity is steady.
- Perfect sink conditions are constantly accomplished in the release climate.

Higuchi was the first to determine a condition to depict the release of a drug from an insoluble framework as the square root of a time-dependent cycle based on Fickian diffusion. The Higuchi equation can be expressed as:

$Q_t = K_H (t)^{1/2}$

Where Qt represents the amount of drug released at time t. KH is the release rate constant for the Higuchi model. When the data is plotted as cumulative drug released versus square root of time, it yields a straight line, showing that medication was delivered by diffusion mechanism. The slope is equal to 'KH'.

Korsmeyer-Peppas Model

To understand the dissolution mechanisms from the network, the delivery information was fitted utilizing the notable observational condition proposed by Korsmeyer and Peppas. Korsmeyer and Peppas proposed a fundamental relationship to describe drug release from a polymeric system, which follows a specific type of dissolution mechanism. They represented this relationship with the following equation:

$Mt/M\infty = Kkpt\ n$

Where,

$Mt/M\infty$ is a fraction of drug released at time t,

$\log (Mt/M\infty) = \log Kkp + n \log t$,

Mt represents the amount of drug released at time t,

$M\infty$ is the total amount of drug released after an infinite amount of time

n is the diffusional exponent, also known as the drug release exponent,

Kkp is the Korsmeyer release rate constant. To study release kinetics a graph is plotted between log cumulative % drug release log (Mt /M∞) vs. log time (log t).

Hixson Crowell model.

The Hixson-Crowell cube root law describes drug release from systems where there is a change in the surface area and diameter of particles or tablets over time Thus, particles of normal territory are relative to the cube root of its volume. From the above idea Hixson-Crowell set up a connection between drug delivery and time which can be addressed by equation as

$W_0^{1/3} - Wt^{1/3} = \kappa_{hct}\ t$

Where,

W0 is the initial amount of drug in the pharmaceutical dosage form (Amount of drug remaining at time 0)

Wt is the remaining amount of drug in the pharmaceutical dosage form at time t;

Khct is the Hixson-Crowell constant which describes the relationship between surface area and volume.

Table 2: Comparison of F-7 Nanogel with marketed formulation

Time in hours	F-7	Marketed formulation
0	0	0.0
1	6.11	4.26
2	10.42	7.24
3	15.74	9.32
4	20.13	14.14
5	27.25	20.26
6	33.74	26.42
7	39.76	32.83
8	46.29	37.38
9	52.61	45.26
10	57.69	53.38
11	63.57	59.17
12	69.35	65.99
13	74.67	65.37
14	83.53	81.25
15	87.24	85.43
16	94.85	91.93
17	95.89	92.31

To study the release kinetics, a graph is plotted between the cube root of the percentage of drug remaining in the tablet versus time. This helps in understanding the release behavior, particularly in systems where the particle or tablet surface area changes as the drug is released.

***In vitro* Release studies:**

The drug release from the formulation was determined by using the apparatus known as Franz Diffusion Cell, which consist of a cylindrical glass tube which was opened at both the ends. 1 gm of gel equivalent to 10 mg of Oxaprozin was spread uniformly on the surface of cellophane membrane (previously soaked in medium for 24 hrs.) and was fixed to the one end of tube. The whole assembly was fixed in such a way that the lower end of tube containing gel was just touches (1-2 mm deep) the surface of diffusion medium i.e. 100 ml of pH 6.8 phosphate buffer contained in 100 ml beaker. The assembly was positioned on a thermostatic hot plate with a magnetic stirrer and maintained at a temperature of 37°C ± 2°C. The contents were stirred using a magnetic bar at 100 rpm for a specified period of time of 24 hrs., 5 ml of samples were withdrawn at different time intervals [15] and recorded data on UV-Visible spectroscopy for oxaprozin was 285 nm and 226 nm for ibuprofen gel formulation [16-17]. The same procedure should be applied for the market formulation as per protocol and observed data has been reported in result and discussion data.

RESULT AND DISCUSSION

***In-vitro* drug release kinetic of optimized formulation**

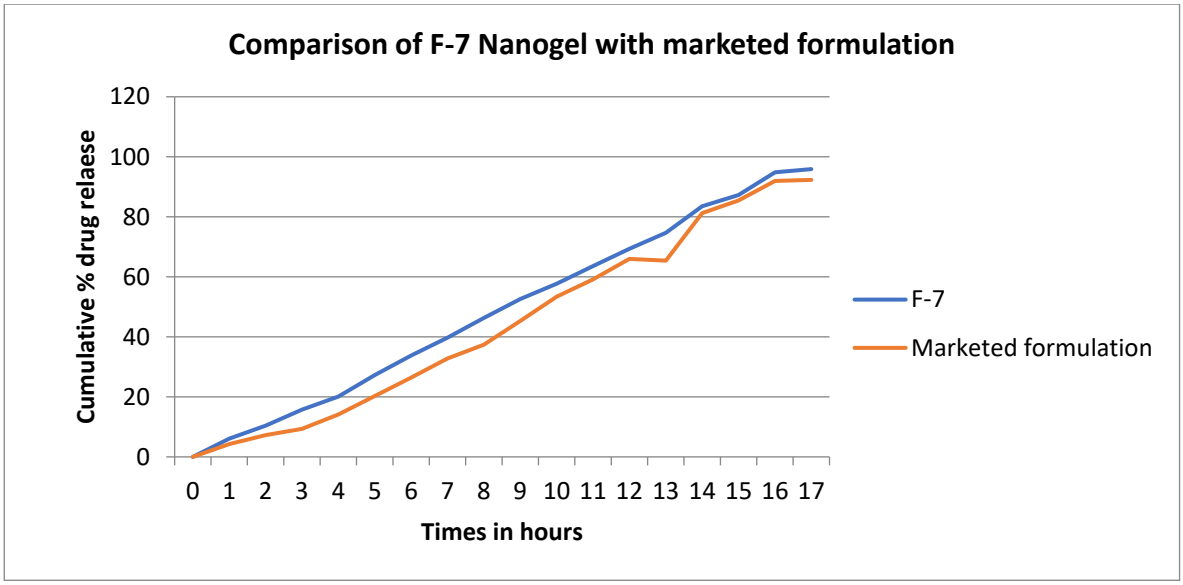
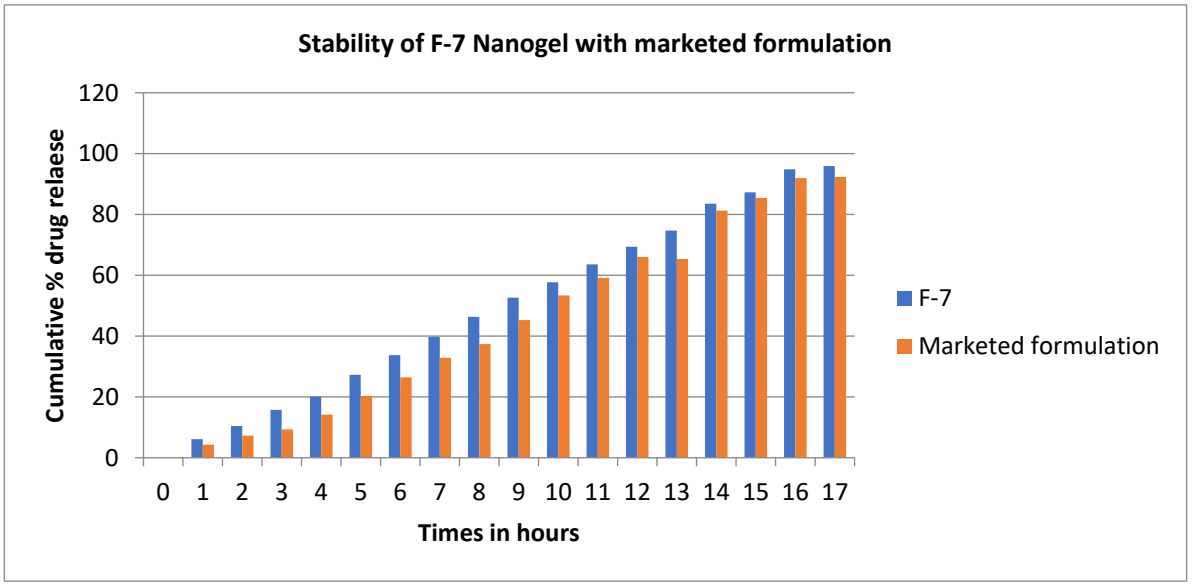


Figure 6: Comparison of F-7 Nanogel with marketed formulation



**Data recorded after 3 months after formulation and 3-month-old market formulation of market batch*

Figure 7: Stability study for Comparison of F-7 Nanogel with marketed formulation

To understand the mechanism by which the medication was delivered from the drug in formulation F7, various release kinetics model including zero order, first order, Higuchi and Korsmeyer-Peppas model were applied as shown in Figure. Numerical models are regularly used to anticipate the delivery system and analyze release profile. For all the optimized formulations, the % drug release vs time (zero order), log percent drug remaining vs time (first order), log per cent drug release vs square root of time (Higuchi plot), log of log % drug release vs. log time (Korsmeyer and Peppas Exponential Equation) and cube root of initial drug concentration - cube root of fraction of drug remaining vs time (Hixson Crowell plot) were plotted.

In each situation, R^2 value was determined from the chart and detailed. Zero order release kinetics was found (R^2=0.992) to fit the release data best.

Comparison with market product with formulated nanogel F-7:

Brand names: Ibugic Gel
Mfg. by: Cipla
Dosage form: Gel

CONCLUSION

Preparation of Oxaprozin Nanogel prepared at different concentration of excipients for batch A, batch B and Batch C and the formulated nanogel was optimized F7 formulation considered as best formulation in batch-C from all formulation. The information acquired from ex vivo permeation studies were plotted in various models of data treatment and compared with market formulation Ibugic gel manufactured by Cipla pharmaceutical Ltd. Data observed as drug release kinetics studies in each situation, R^2 value was determined from the chart and detailed. Zero order release kinetics was found (R^2=0.992) to fit the release data best and the % drug release for optimized up to 17 hours of F-7 formulation was found 95.89% which was higher than

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Conflict of interest; NIL

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