Original Article

# Release kinetic study of enteric coating of senna tablet

**Ramchander Khatri [1], Tanuj Hooda[1], Rakesh Gupta[2], Prashant Kumar[1], Pawan Jawal[3]**

[1]Department of Pharmacognosy, Vaish Institute of Pharmaceutical Education & Research, Rohtak, Haryana, India, [2]Department of Pharmaceutical Chemistry, Vaish Institute of Pharmaceutical Education & Research, Rohtak, Haryana, India, [3]Department of Pharmaceutics, S.B.M.N Institute of Pharmaceutical Science & Research, Rohtak, Haryana, India

**Correspondence:**
Ramchander khatri, Vaish Institute of Pharmaceutical Education & Research, Rohtak - 124 001, Haryana, India. Phone: +91-9896563483.
E-mail: rckhatri@gmail.com

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## ABSTRACT

The development of enteric coated formulation has been one approach to preventing the drug from coming into contact with gastric mucosa. The enteric coating dosage form releases the drug after leaving the stomach. The results of this study indicate that enteric coated tablets using 12% cellulose acetate phthalate (CAP) are suitable for the senna drug which is mainly active in the lower Gastrointestinal track. The physical compatibility study at 40°C/75% RH showed that senna extract, ajowan oil, and excipients used during the research work found to be physically compatible. The tablet formulation was prepared by wet granulation technique, and the physical characteristics of granules were evaluated for moisture content (%), compressibility index, angle of repose, Hausner ratio and found to have good flow and compressibility. The tablet formulations developed were found to be within the limits with respect to in-process parameters such as thickness, hardness, friability, weight variation, and disintegration time. The different trail batches of enteric coated tablets were developed using a different percentage of CAP, and drug release profile of different batches were studies with the help of five kinetic models, namely zero order, first order, Higuchi, Hixon-crowell, and Korsmeyer-Peppas model. The entire kinetic models studied for all the batches of different concentration of CAP. The batch containing 4% CAP, it was observed that the batch followed zero-order kinetic model because of having maximum $R^2$ value of 0.990. The batch having 8% CAP and it was observed that the batch followed zero-order kinetic model because of having maximum $R^2$ value of 0.959. The batch having 12% CAP and it was observed that the batch followed Higuchi model because of having maximum $R^2$ value of 0.999. The batch having 16% CAP and it was observed that the batch followed Hixon-Crowell model and Higuchi model both because of having maximum $R^2$ value of 0.991. The batch having 20% CAP, it was observed that the batch followed zero-order kinetic and Higuchi kinetic model because of having maximum $R^2$ value of 0.984. The batch having 24% CAP, it was observed that the batch followed Hixon-Crowell kinetic model because of having maximum $R^2$ value of 0.981.

**Keywords:** Senna, tablet, cellulose acetate phthalate, pharmacokinetic

## INTRODUCTION

Herbal medicines are the product that contains plant materials as their pharmacologically active constituents. They are usually consisting of complex mixtures of more than one plants and plant materials. The plant products have botanical resources such as leaves, flowers, fruits, seeds, stems, woods, barks, roots, rhizomes, or other plant parts. The plant parts as well include gums, essential oils, and resins etc. [1]

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Herbal medicine is also known as phytomedicine/botanical medicine. Recently, the treatment of disease with herbal medicine has been

addressed as phytopharmacon therapy. Moreover, herbal products have been included lately in dietary supplements.[2]

## ROLE OF PLANTS AS HERBAL MEDICINE

All plants generate chemical compounds as part of their normal metabolic activities. These comprise primary metabolites, such as sugars, amino acids and fats, found in all plants, and secondary metabolites such as glycosides, alkaloids, volatile oils, resins, and tannins and phenolic compounds, are present in a slighter range of plants, a few useful ones present merely in a scrupulous genus or species. Pigments harvest light, shield the organism from radiation and show colors to catch the attention of pollinators. Many common weeds have medicinal properties. The chemical summary of a single plant can differ over time as it reacts to changing conditions. It is the secondary metabolites and pigments that can have therapeutic actions in humans and which can be polished to produce drugs.[3]

One of the most popular categories under herbal OTC segment is laxatives which relieve constipation and correct bowel irregularities. Among laxatives, bulk laxatives have largest market size followed by other such as stimulant laxatives, lubricants laxatives, and osmotic laxatives. Senna is the most common stimulant laxatives used as an active ingredient. This ingredient has been choice of researchers; therefore, ample scientific data are available on the same. Senna is official in various pharmacopoeias and also covered by the WHO in its monograph on medicinal plants. Sennosides are the active chemical constituents of senna which is used for the relief of constipation. Sennosides have been reported to induce griping. Due to this side effect, the use of senna has reduced recently. There is a need to address this issue by formulators. Use of carminatives can reduce griping. Carminatives such as mint, cloves, fennel, cumin, and ajowan have been reported to have antispasmodic activity. Among these, carminatives ajowan has much valued for antispasmodic action, Therefore, a combination of senna and ajowan in the form of tablet to provide the benefit of sennosides without griping.[18]

## KINETIC MODELS

In the drug release method, a drug leaves a drug product and is subjected to absorption, distribution, metabolism, and excretion and ultimately becoming accessible for their therapeutic action. The drug release is illustrated in numerous ways. The instantaneous release drug products permit drug molecules to dissolve without the aim of delaying dissolution. The modified release dosage form counting both extended release or delayed drug products. The delayed release is express as the free of a drug at a time other than instantly administration. The extended-release products are designed to formulate the drug offered over a comprehensive period subsequent to administration.[7]

*In vitro* dissolution has been accepted as a significant aspect in drug development. Under assured conditions, it may be employed as substitute to the evaluation of bioequivalence. Various kinetics model explains drug dissolution from immediate and modified release formulation. There are numerous kinetic models to characterize the dissolution profiles of drug.[5]

They play a significant role in the calculation of mechanism of drug release and also give a further general plan for the development of other system. It is well-known that, several successful drug delivery systems developed as a result of almost random selection of components, geometrics, and configuration. Consideration of the modeling and physiological parameters is important for a complete model of drug release. To explain the drug release rate from different drug delivery system a large number of models were developed. Some of the important models are:

- Zero-order kinetic model
- First order kinetic model
- Higuchi kinetic model
- Korsmeyer-Peppas kinetic model
- Hixon-Crowell kinetic model

## ZERO ORDER KINETIC MODEL[6]

Zero-order explains the method in which the release rate of the drug is independent of its concentration. The equation is:

$$C=C_0-K_0 t$$

Where,
C=Amount of drug release or dissolved
$C_0$=Initial amount of the drug in solution
$K_{0=}$Zero-order rate constant
t=Time

To study the release kinetics, the graph is plotted between cumulative amounts of drug released versus time.

### Application

The relationship may be apply to explain the drug dissolved of the drug from numerous types of the modified release pharmaceutical dosage form as in the case of various transdermal system and matrix tablet with low soluble drugs in coated forms.

## FIRST ORDER KINETIC MODEL[9]

This model is applied to illustrate the absorption and elimination of various drugs. Although it is difficult to the mechanism on the hypothetical basis. In this case, drug release rate is depend on the concentration; that may be represented in decimal logarithm as:

$$\text{Log } C=\text{Log } C_0-Kt/2.303$$

Where,
$C_0$=Initial drug concentration
K=First order constant
t=Time

The data received are plotted as log cumulative percentage of drug remaining versus time, which give way a straight line through slop= K/2.303.

### Applications

This relationship could be used to explain the drug dissolved in dosage forms like those contained water-soluble drugs in porous material.

## HIGUCHI KINETIC MODEL[13]

Higuchi published the possibly mainly renowned and most frequently applied mathematical equation to explain the release of drug release from matrix system. This model is regularly applicable to the dissimilar geometrics and porous system and to learn the release of water-soluble and low soluble drugs incorporated in semisolid and solid matrices.[10]

The basic equation of Higuchi model is

$$C=[D\ (2qt-Cs)\ Cst]^{1/2}$$

Where
C=Amount of drug release per unit area of the matrix ($mg/cm^2$)
D=Diffusion coefficient of the drug in the matrix ($mg/cm^2$)
Qt=Total amount of drug in a unit volume of matrix ($mg/cm^3$)
Cs=Dimensional solubility of drug in the polymer matrix ($mg/cm^3$)
t=Time (h)

The data received were plotted as cumulative percentage of drug release versus square root of time

### Application

This model dissolution of drug from several modified release dosage form like some transdermal system and matrix tablet with water-soluble drugs are studied.[12]

## KORSMEYER-PEPPAS KINETIC MODEL[15]

This model derived a simple connection which describes the release of drug from a polymeric system to illustrate the mechanism of drug release, first 60% of the drug release data were fixed in this model.

$$Ct/C\infty=kt^n$$

Where,
Ct/C∞=Portion of drug release at time "t"
K=Rate constant
n=Release exponent

A customized form of this equation was developed to regulate the log time (l) in the commencement of release of drug from the dosage form.

$$C_{(t-l)}/C\infty=a\ (t-l)^n$$

Where there is chance of a burst effect, b this equation becomes

$$Ct/C\infty=at^n+b$$

In the absence of lag time or burst effect l and "b" values would be zero and only at n is used.[8]

The plot made by log cumulative percentage of drug release versus log time.

### Application

This model is expressed the drug release from several modified release dosages form.

## HIXON-CROWELL KINETIC MODEL[4]

To evaluate the release of drugs with vary in the surface area and the diameter of the particles and tablet formulation this model was recognized that the regular area of particles is relative to the cubic root of its volume. It is possible to derive an equation for a drug powder containing uniform size particles which describe the rate of dissolution based on the cube root of particles. The equation is:

$$C_0^{1/3}-C_t^{1/3}=K_{HC}t$$

Where,
$C_t$=Amount of drug released in time "t"
$C_0$=Amount of drug in the tablet (Initial)
$K_{HC}$=Rate constant for Hixon-Crowell equation.

Graph plot in between cube root of drug percentage remaining in the matrix versus time.

### Application

This is appropriate to dosages form like tablet; in which the dissolution happens in planes which is parallel to drug surface if dimensions of the tablet reduce proportionality, in such a way that the primary geometry form remain steady all the time (metabolite) may excrete out from breast milk to the infants (0.01% of the total amount taken). In feeding women, the active constituents generally enter in the milk but are not sufficient to induce diarrhea in the infants.[14]

## EXPERIMENT WORK

### Enteric coating of senna tablet

#### *Preparation of enteric coating solution*

The enteric coating solutions were prepared using cellulose acetate phthalate (CAP) in different concentration such 4%, 8%, 12%, 16%, 20%, and 24%. The CAP was dissolved in ethyl alcohol, sorbitan monooleate and part of acetone. To make sure appropriate spreading, the dye, titanium dioxide, and talc were appropriately dispersed in acetone. After that, the color solution was added to the coating solution.

#### *Coating process*

The enteric coating of optimized batch of senna tablet was done by conventional rotating pan using different concentration of CAP. The

required amount of the coating solution was sprayed on pre-warmed tablet bed in a pan coater. The tablets are dried with the help of inlet air having temperature 40°C to 50°C.[17] The coating process is repeated till the desired level of coating was achieved.[19-21]

Formulation of enteric coating solution [Table 1].

Trial batch of different percentage of CAP for the enteric coated tablet of senna [Table 2].

## RESULTS [TABLES 3 AND 4]

Cumulative drug release profile of enteric coated senna tablet [Table 5 and Figure 1]

### Study of release kinetics of all the batches

The data obtained from *in vitro* dissolution studies were fitted in different models to determine the mechanism of drug release.

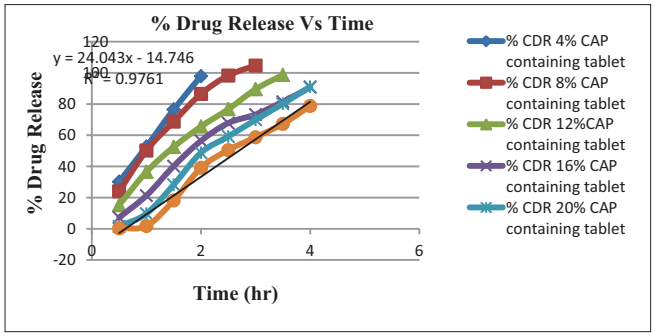


**Figure 1:** Cumulative % cumulative drug release profile of different batches of senna tablet

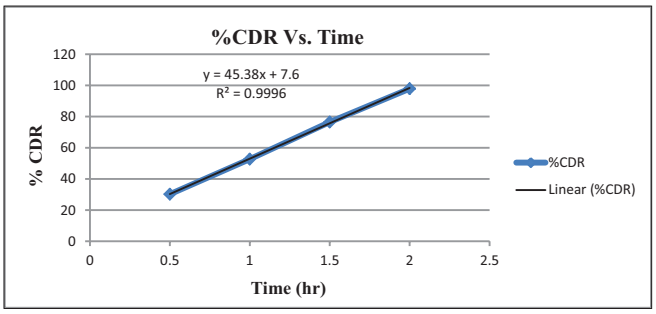


**Figure 2:** Senna release kinetic of 4% cellulose acetate phthalate according to zero-order kinetic

- Zero-order kinetic model
- First-order kinetic model
- Higuchi kinetic model
- Hixon-Crowell kinetic model
- Korsmeyer-Peppas kinetic model

Various kinetic models of all the formulations are shown in following Figures 2-31.

Study of release kinetics of batch having 4% CAP [Table 6 and Figures 2-6].

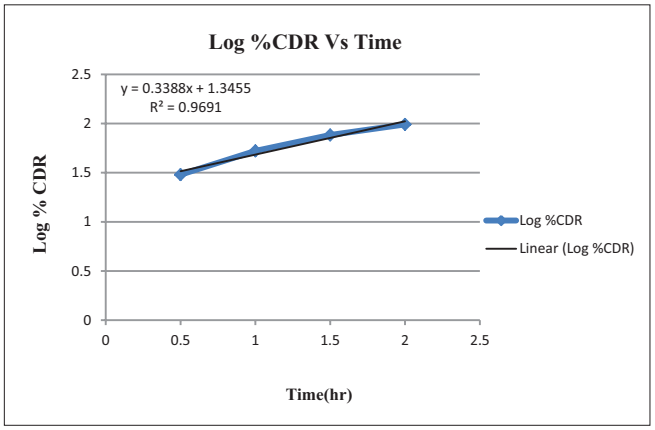


**Figure 3:** Senna release kinetic of 4% cellulose acetate phthalate according to first order kinetic

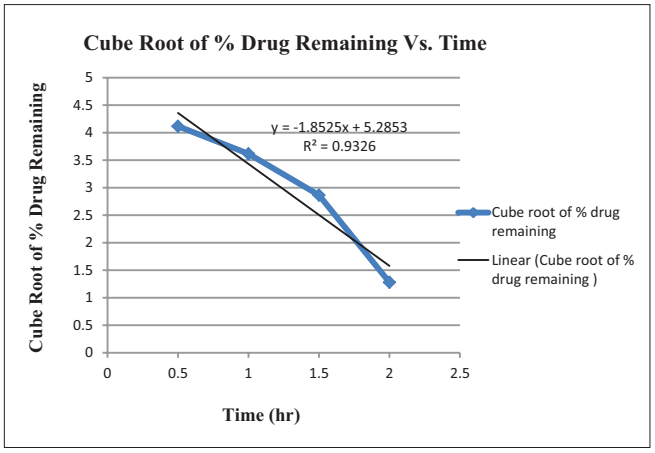


**Figure 4:** Senna release kinetic of 4% cellulose acetate phthalate according to Hixon-Crowell kinetic

**Table 1: Formula for enteric coating solution**

| Ingredients (%) | ECT$^{-1}$ | ECT$^{-2}$ | ECT$^{-3}$ | ECT$^{-4}$ | ECT$^{-5}$ | ECT$^{-6}$ | ECT$^{-7}$ |
|---|---|---|---|---|---|---|---|
| Cellulose acetate phthalate | 4 | 8 | 12 | 16 | 18 | 20 | 24 |
| Propylene glycol | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| Ethyl alcohol | 40 | 40 | 40 | 40 | 40 | 40 | 40 |
| Sorbitan mono oleate (span-80) | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 |
| Dye (Neelicol Ponceau 4R) | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Talc | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Titanium oxide | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Acetone | q.s to 100% | q.s to 100% | q.s to 100% | q.s to 100% | q.s to 100% | q.s to 100% | q.s to 100% |

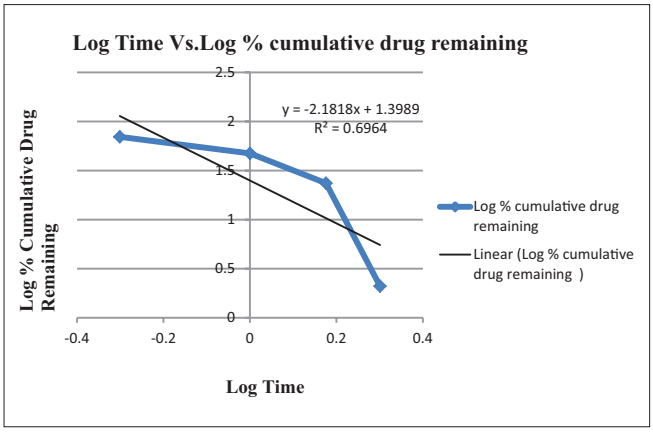


**Figure 5:** Senna release kinetic of 4% cellulose acetate phthalate according to Korsmeyer-Peppas kinetic

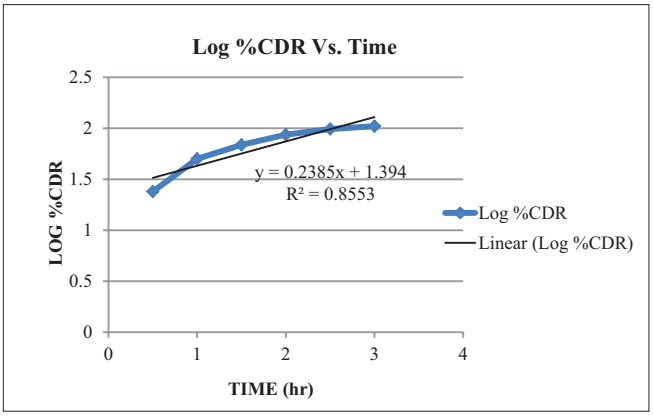


**Figure 8:** Senna release kinetic of 8% cellulose acetate phthalate according to first order kinetic

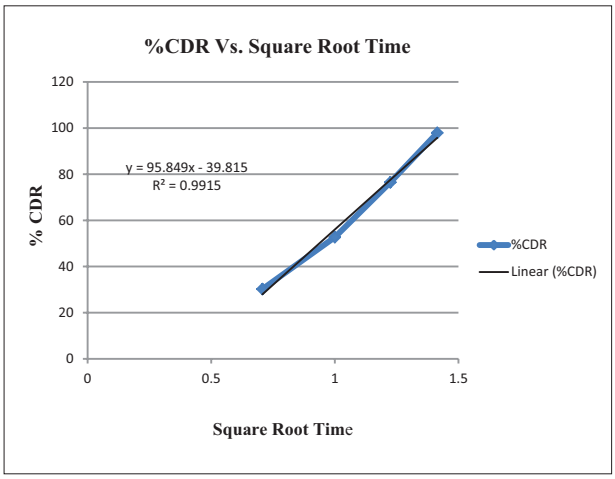


**Figure 6:** Senna release kinetic of 4% cellulose acetate phthalate according to Higuchi kinetic

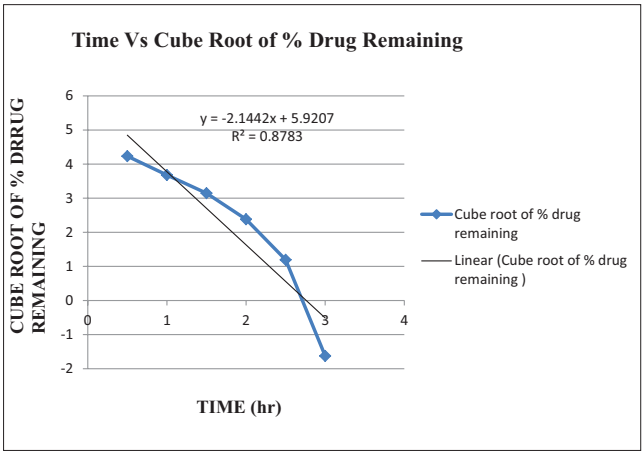


**Figure 9:** Senna release kinetic of 8% cellulose acetate phthalate according to Hixon-Crowell

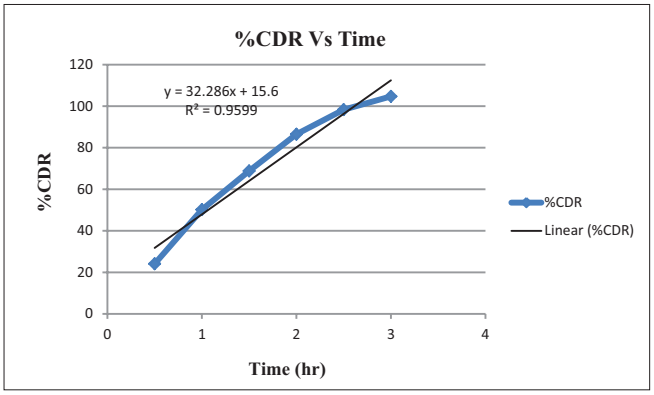


**Figure 7:** Senna release kinetic of 8% cellulose acetate phthalate according to zero-order kinetic

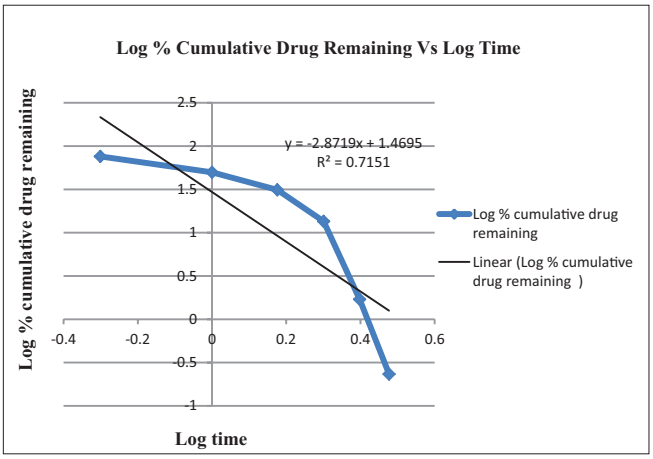


**Figure 10:** Senna release kinetic of 8% cellulose acetate phthalate according to Korsmeyer-Peppas kinetic

The statistical kinetics values for the batch 4% CAP is represented in Table 7.

*In vitro* drug release parameters for 8% CAP [Table 8 and Figures 7-11].

The statistical kinetics values for the batch having 8% CAP is represented in Table 9.

*In vitro* drug release parameters for 12% CAP [Table 10 and Figures 12-16].

**Table 2:Trail batches of different % of cellulose acetate phthalate**

| Trial batch excipients (mg) | $RCSA_1$ | $RCSA_2$ | $RCSA_3$ | $RCSA_4$ | $RCSA_5$ | $RCSA_6$ |
|---|---|---|---|---|---|---|
| Cellulose acetate phthalate | 24 | 48 | 72 | 96 | 120 | 144 |
| Senna extract | 150 | 150 | 150 | 150 | 150 | 150 |
| Ajowan oil | 36 | 36 | 36 | 36 | 36 | 36 |
| β-cyclodextrin | 64 | 64 | 64 | 64 | 64 | 64 |
| Microcrystalline cellulose (PH 101) | 135 | 111 | 87 | 63 | 39 | 15 |
| Croscarmellose sodium | 35 | 35 | 35 | 35 | 35 | 35 |
| Microcrystalline cellulose (PH 102) | 14 | 14 | 14 | 14 | 14 | 14 |
| PVP | 40 | 40 | 40 | 40 | 40 | 40 |
| Calcium carbonate | 20 | 20 | 20 | 20 | 20 | 20 |
| Pre-gelatinized starch | 60 | 60 | 60 | 60 | 60 | 60 |
| Talc | 9 | 9 | 9 | 9 | 9 | 9 |
| Magnesium stearate | 9 | 9 | 9 | 9 | 9 | 9 |
| Aerosil | 4 | 4 | 4 | 4 | 4 | 4 |
| Total weight in (mg) | 600 | 600 | 600 | 600 | 600 | 600 |

**Table 3: Effect of different % of cellulose acetate phthalate on disintegration time in different disintegration media**

| Parameters | 4% CAP tablet | 8% CAP tablet | 12% CAP tablet | 16% CAP tablet | 20% CAP tablet | 24% CAP tablet |
|---|---|---|---|---|---|---|
| DT in 0.1 N HCl | Disintegrate | Disintegrate | Unchanged after 2 h | Unchanged after 2 h | Unchanged after 2 h | Unchanged after 2 h |
| DT in phosphate buffer (pH 6.8) | 50 min 55 s | 59 min 15 s | 76 min 50 s | 90 min 10 s | 108 min 25 s | 124 min 20 s |

CAP: Cellulose acetate phthalate

**Table 4: Characteristics of senna tablets after enteric coating**

| Parameters | 4% CAP tablet | 8% CAP tablet | 12% CAP tablet | 16%CAP tablet | 20% CAP tablet | 24%CAP tablet |
|---|---|---|---|---|---|---|
| DT | 50 min 55 s | 59 min 15 s | 76 min 50 s | 90 min 10 s | 108 min 25 s | 124 min 20 s |
| % age drug release after 2 h | 97.9 | 86.5 | 65.6 | 56.4 | 48.8 | 39.2 |
| Drug contents | 127% | 114% | 96% | 85% | 78% | 55% |

CAP: Cellulose acetate phthalate

**Table 5: % age CDR of various batches of enteric coated senna tablet containing cellulose acetate phthalate**

| Time (h) | % CDR | | | | | |
|---|---|---|---|---|---|---|
| | 4% CAP | 8% CAP | 12% CAP | 16% CAP | 20% CAP | 24% CAP |
| 0.5 | 30.2 | 24.1 | 15.2 | 7.2 | 1.5 | 0.3 |
| 1.0 | 52.7 | 50.2 | 36.5 | 21.3 | 9.7 | 1.8 |
| 1.5 | 76.5 | 68.8 | 52.5 | 40.2 | 28.3 | 18.2 |
| 2.0 | 97.9 | 86.5 | 65.6 | 56.4 | 48.8 | 39.2 |
| 2.5 | | 98.3 | 76.7 | 67.8 | 59.2 | 50.5 |
| 3.0 | | 104.7 | 89.5 | 73.3 | 69.9 | 58.7 |
| 3.5 | | | 98.7 | 81.5 | 80.2 | 67.3 |
| 4.0 | | | | 90.7 | 91.1 | 78.8 |

CAP: Cellulose acetate phthalate, CDR: Cumulative drug release

**Table 6: *In vitro* drug release parameters for 4% cellulose acetate phthalate**

| Time (h) | %CDR | Log %CDR | Cube root of % drug remaining | Log % cumulative drug remaining | Square root time | Log time |
|---|---|---|---|---|---|---|
| 0.5 | 30.2 | 1.4800 | 4.1173 | 1.8438 | 0.7071 | −0.3010 |
| 1.0 | 52.7 | 1.7218 | 3.6164 | 1.6748 | 1.00 | 0.00 |
| 1.5 | 76.5 | 1.8836 | 2.8643 | 1.3710 | 1.2247 | 0.1760 |
| 2.0 | 97.9 | 1.9907 | 1.2805 | 0.3222 | 1.4142 | 0.3010 |
| 2.5 | | | | | 1.5811 | 0.3979 |
| 3.0 | | | | | 1.7320 | 0.4771 |
| 3.5 | | | | | 1.8708 | 0.5440 |
| 4.0 | | | | | 2.00 | 0.6020 |

CDR: Cumulative drug release

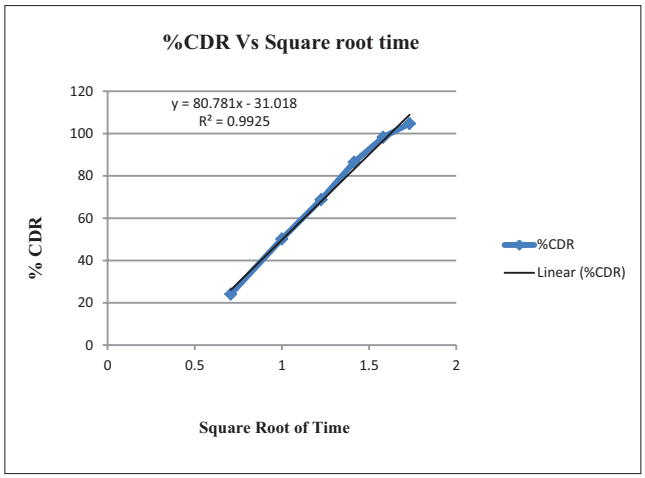


**Figure 11:** Senna release kinetic of 8% cellulose acetate phthalate according to Higuchi kinetic

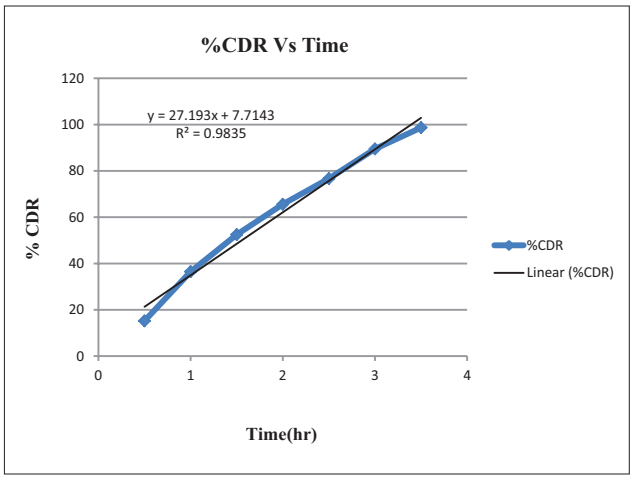


**Figure 12:** Senna release kinetic of 12% cellulose acetate phthalate according to zero-order kinetics

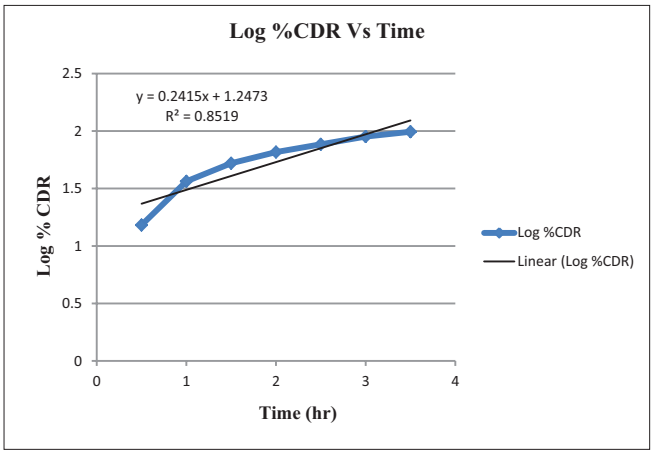


**Figure 13:** Senna release kinetic of 12% cellulose acetate phthalate according to first order kinetic

The statistical kinetics values for the batch having 12% CAP is represented in Table 11.

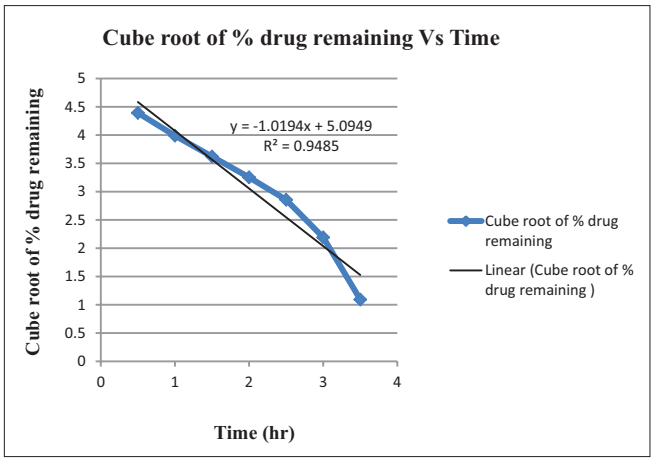


**Figure 14:** Senna release kinetic of 12% cellulose acetate phthalate according to Hixon-Crowell

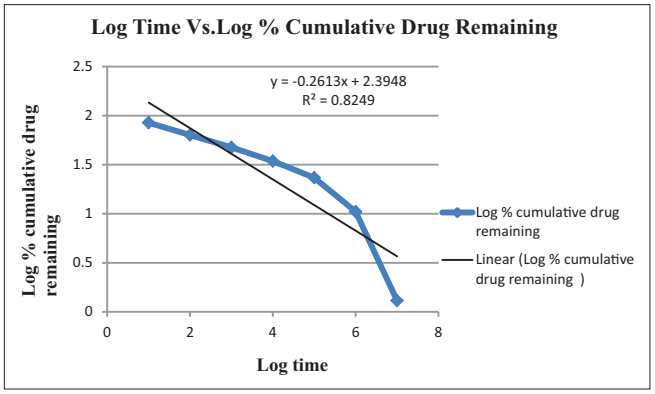


**Figure 15:** Senna release kinetic of 12% cellulose acetate phthalate according to Korsmeyer-Peppas kinetic

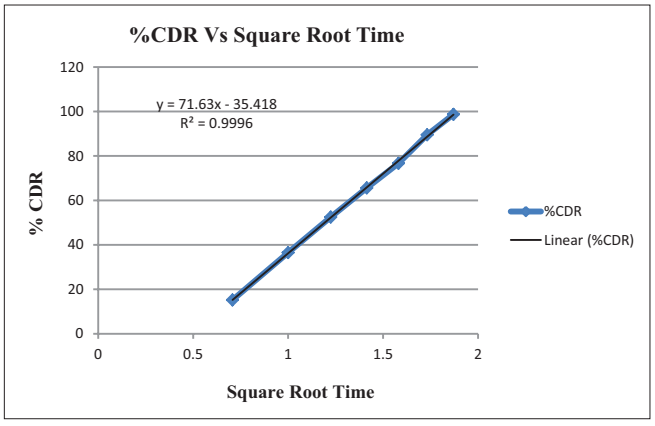


**Figure 16:** Senna release kinetic of 12% cellulose acetate phthalate according to Higuchi kinetic

*In vitro* drug release parameters for 16% CAP [Table 12 and Figures 17-21].

The statistical kinetics values for the batch 16% CAP is represented in Table 13.

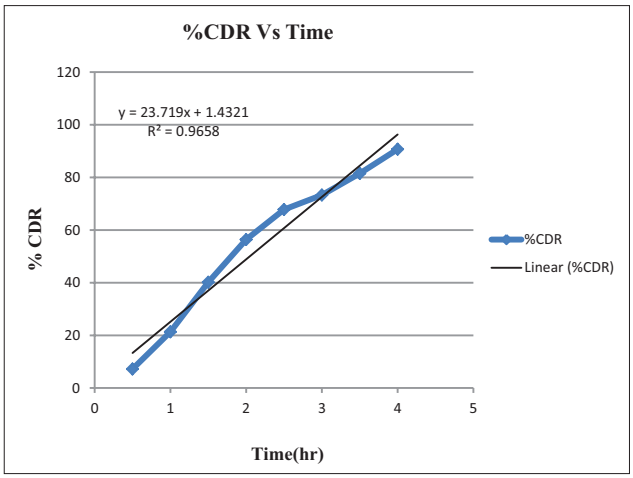


**Figure 17:** Senna release kinetic of 16% cellulose acetate phthalate according to zero-order kinetic

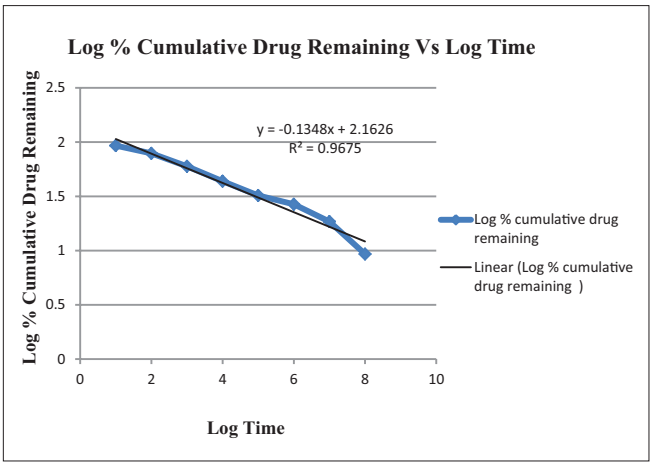


**Figure 20:** Senna release kinetics of 16% cellulose acetate phthalate according to Korsmeyer-Peppas kinetic

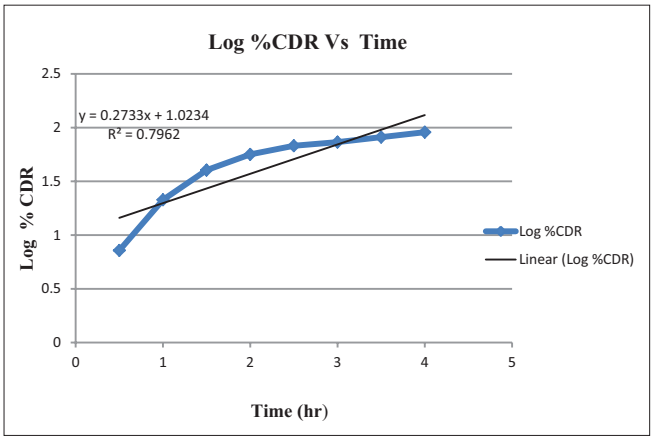


**Figure 18:** Senna release kinetics of 16% cellulose acetate phthalate according to first order kinetics

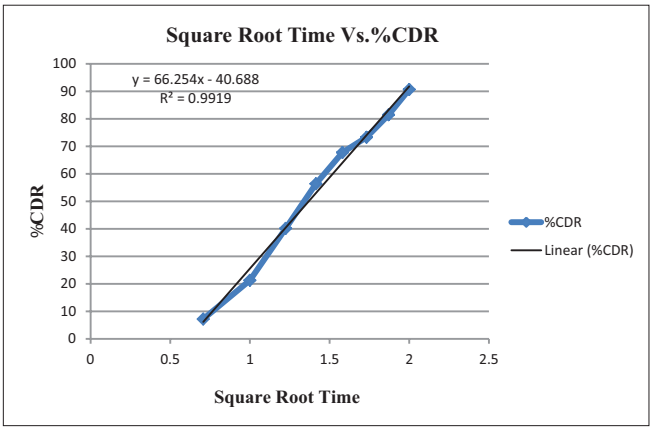


**Figure 21:** Senna release kinetic of 16% cellulose acetate phthalate according to Higuchi kinetic

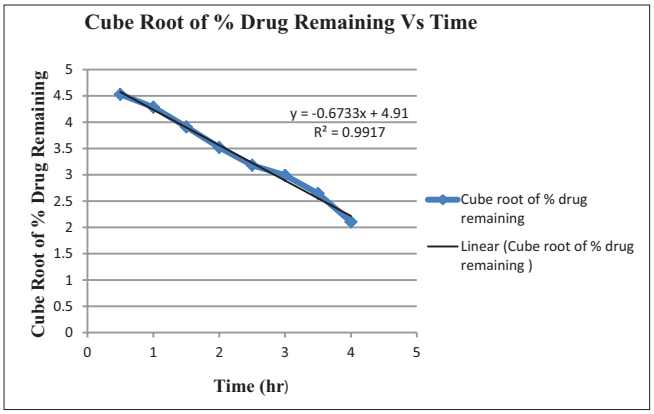


**Figure 19:** Senna release kinetic of 16% cellulose acetate phthalate according to Hixon-Crowell kinetic

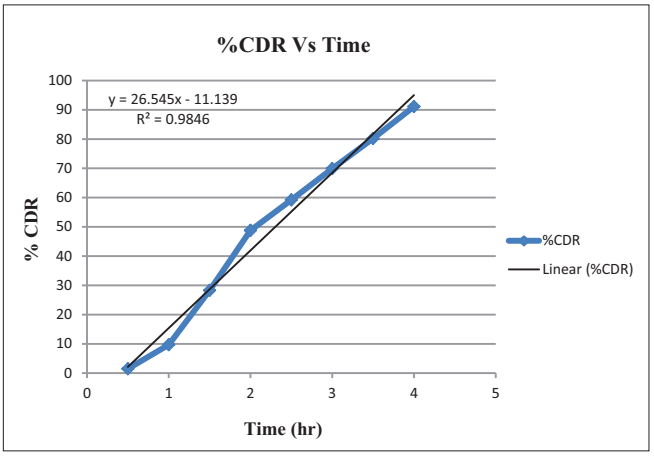


**Figure 22:** Senna release kinetic of 20% cellulose acetate phthalate according to zero-order kinetic

*In vitro* drug release parameters for 20% CAP [Table 14 and Figures 22-26].

The statistical kinetics values for the batch having 20% CAP is represented in Table 15.

**Table 7: Statistical kinetics values for batch 4% CAP**

| Kinetic models | $R^2$ | Slope |
|---|---|---|
| Zero order | 0.999 | 45.38 |
| First order | 0.969 | 0.338 |
| Hixon-Crowell | 0.932 | −1.852 |
| Korsmeyer-Peppas | 0.696 | −2.181 |
| Higuchi kinetic | 0.991 | 95–84 |

Among the entire kinetics model studied for batch having 4% CAP, it was observed that the batch followed Zero order kinetic model because of having maximum $R^2$ value of 0.990 (close to 1.0)

**Table 8: *In vitro* drug release parameters for 8% cellulose acetate phthalate**

| Time (h) | %CDR | Log %CDR | Cube root of % drug remaining | Log % cumulative drug remaining | Square root time | Log time |
|---|---|---|---|---|---|---|
| 0.5 | 24.1 | 1.3802 | 4.2339 | 1.8802 | 0.7071 | −0.3010 |
| 1.0 | 50.2 | 1.7007 | 3.6791 | 1.6972 | 1.00 | 0.00 |
| 1.5 | 68.8 | 1.8375 | 3.1481 | 1.4941 | 1.2247 | 0.1760 |
| 2.0 | 86.5 | 1.9370 | 2.3811 | 1.1303 | 1.4142 | 0.3010 |
| 2.5 | 98.3 | 1.9925 | 1.1934 | 0.2304 | 1.5811 | 0.3979 |
| 3.0 | 104.7 | 2.0199 | −1.6261 | −0.6334 | 1.7320 | 0.4771 |
| 3.5 | | | | | 1.8708 | 0.5440 |
| 4.0 | | | | | 2.00 | 0.6020 |

CDR: Cumulative drug release

**Table 9: Statistical kinetics values for batch 8% CAP**

| Kinetic models | $R^2$ | Slope |
|---|---|---|
| Zero order | 0.959 | 32.28 |
| First order | 0.855 | 0.238 |
| Hixon-Crowell model | 0.878 | −2.1444 |
| Korsmeyer-Peppas model | 0.715 | −2.871 |
| Higuchi model | 0.992 | 80.87 |

Among the entire kinetics model studied for batch having 8% CAP, it was observed that the batch followed zero-order kinetic model because of having maximum $R^2$ value of 0.959 (close to 1.0). CAP: Cellulose acetate phthalate

**Table 10: *In vitro* drug release parameters for 12% cellulose acetate phthalate**

| Time (h) | %CDR | Log %CDR | Cube root of % drug remaining | Log % cumulative drug remaining | Square root time | Log time |
|---|---|---|---|---|---|---|
| 0.5 | 15.2 | 1.18184 | 4.3933 | 1.92839 | 0.7071 | −0.3010 |
| 1.0 | 36.5 | 1.56229 | 3.9895 | 1.80277 | 1.00 | 0.00 |
| 1.5 | 52.5 | 1.72015 | 3.6215 | 1.67699 | 1.2247 | 0.1760 |
| 2.0 | 65.6 | 1.81690 | 3.2522 | 1.53655 | 1.4142 | 0.3010 |
| 2.5 | 76.7 | 1.88479 | 2.8561 | 1.36735 | 1.5811 | 0.3979 |
| 3.0 | 89.5 | 1.95182 | 2.1897 | 1.02118 | 1.7320 | 0.4771 |
| 3.5 | 98.7 | 1.99431 | 1.0913 | 0.11394 | 1.8708 | 0.5440 |
| 4.0 | | | | | 2.00 | 0.6020 |

CDR: Cumulative drug release

**Table 11: Statistical kinetics values for batch 12% cellulose acetate phthalate**

| Kinetic models | $R^2$ | Slope |
|---|---|---|
| Zero order | 0.983 | 27.19 |
| First order | 0.851 | 0.241 |
| Hixon-Crowell model | 0.948 | −1.019 |
| Korsmeyer-Peppas model | 0.824 | −0.261 |
| Higuchi model | 0.999 | 71.63 |

Among the entire kinetics model studied for batch having 12% CAP, it was observed that the batch followed Higuchi model because of having maximum $R^2$ value of 0.999 (close to 1.0)

**Table 12: *In vitro* release parameters for 16% cellulose acetate phthalate**

| Time (h) | %CDR | Log %CDR | Cube root of % drug remaining | Log % cumulative drug remaining | Square root time | Log time |
|---|---|---|---|---|---|---|
| 0.5 | 7.2 | 0.85733 | 4.5274 | 1.96754 | 0.7071 | −0.3010 |
| 1.0 | 21.3 | 1.32837 | 4.2854 | 1.89597 | 1.00 | 0.00 |
| 1.5 | 40.2 | 1.60422 | 3.9105 | 1.77670 | 1.2247 | 0.1760 |
| 2.0 | 56.4 | 1.75127 | 3.5196 | 1.63948 | 1.4142 | 0.3010 |
| 2.5 | 67.8 | 1.83122 | 3.1814 | 1.50785 | 1.5811 | 0.3979 |
| 3.0 | 73.3 | 1.86510 | 2.9888 | 1.42651 | 1.7320 | 0.4771 |
| 3.5 | 81.5 | 1.91115 | 2.6447 | 1.26717 | 1.8708 | 0.5440 |
| 4.0 | 90.7 | 1.95760 | 2.1029 | 0.96848 | 2.00 | 0.6020 |

CDR: Cumulative drug release

**Table 13: Statistical kinetics values for batch 16% CAP**

| Kinetic models | $R^2$ | Slope |
|---|---|---|
| Zero order | 0.965 | 23.71 |
| First order | 0.796 | 0.273 |
| Hixon-Crowell model | 0.991 | −0.673 |
| Korsmeyer-Peppas model | 0.967 | −0.134 |
| Higuchi model | 0.991 | 66.25 |

Among the entire kinetics model studied for batch 16% CAP, it was observed that the batch followed Hixon-Crowell model and Higuchi model both because of having maximum $R^2$ value of 0.991 (close to 1.0). CAP: Cellulose acetate phthalate

**Table 14: *In vitro* drug release parameters for 20% cellulose acetate phthalate**

| Time (h) | %CDR | Log %CDR | Cube root of % drug remaining | Log % cumulative drug remaining | Square root time | Log time |
|---|---|---|---|---|---|---|
| 0.5 | 1.5 | 0.17609 | 4.61826 | 1.99343 | 0.7071 | −0.3010 |
| 1.0 | 9.7 | 0.98677 | 4.48637 | 1.95568 | 1.00 | 0.00 |
| 1.5 | 28.3 | 1.45178 | 4.15438 | 1.85551 | 1.2247 | 0.1760 |
| 2.0 | 48.8 | 1.68841 | 3.71327 | 1.70926 | 1.4142 | 0.3010 |
| 2.5 | 59.2 | 1.77232 | 3.44260 | 1.61066 | 1.5811 | 0.3979 |
| 3.0 | 69.9 | 1.84447 | 3.11068 | 1.47856 | 1.7320 | 0.4771 |
| 3.5 | 80.2 | 1.90417 | 2.70533 | 1.29666 | 1.8708 | 0.5440 |
| 4.0 | 91.1 | 1.95951 | 2.07235 | 0.94939 | 2.00 | 0.6020 |

CDR: Cumulative drug release

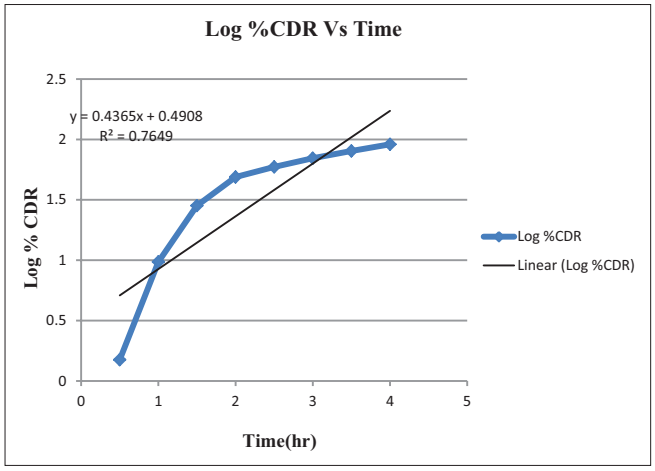


**Figure 23:** Senna release kinetic of 20% cellulose acetate phthalate according to first order kinetic

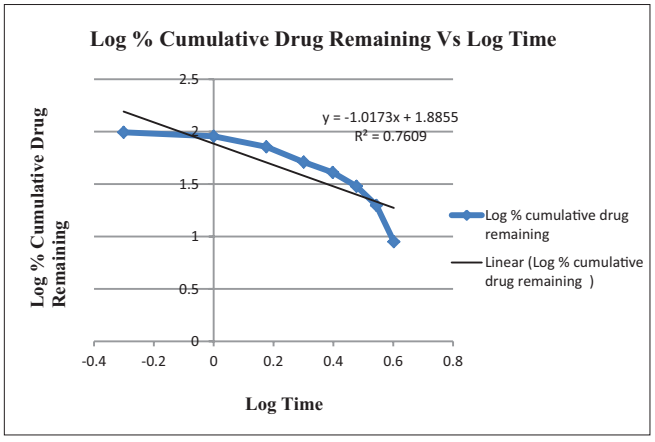


**Figure 25:** Senna release kinetic of 20% cellulose acetate phthalate according to Korsmeyer-Peppas kinetic

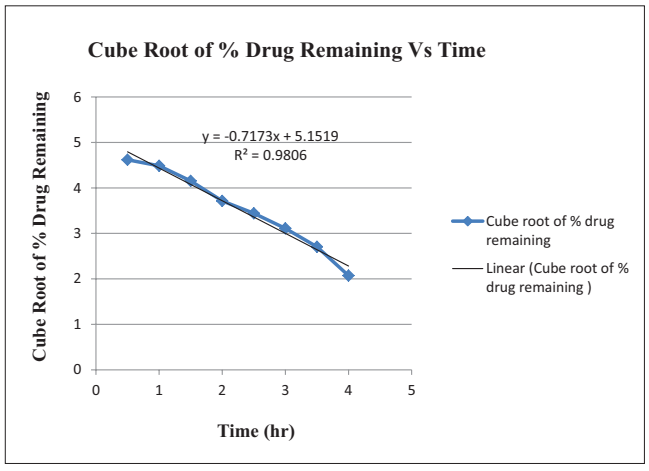


**Figure 24:** Senna release kinetic of 20% cellulose acetate phthalate according to Hixon-Crowell kinetic

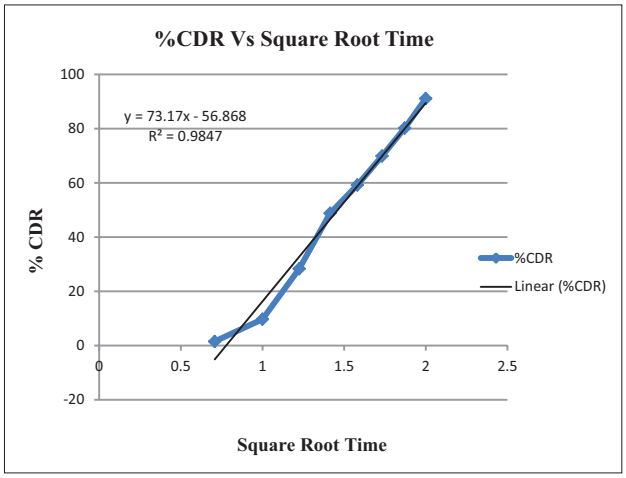


**Figure 26:** Senna release kinetic of 20% cellulose acetate phthalate according to Higuchi kinetic

**Table 15: Statistical kinetics values for batch 20% CAP**

| Kinetic models | $R^2$ | Slope |
|---|---|---|
| Zero order | 0.984 | 26.54 |
| First order | 0.764 | 0.436 |
| Hixon-Crowell model | 0.980 | −0.717 |
| Korsmeyer-Peppas model | 0.760 | −1.017 |
| Higuchi model | 0.984 | 73.73 |

Among the entire kinetics models studied for batch having 20% CAP, it was observed that the batch followed zero order kinetic and Higuchi kinetic model because of having maximum $R^2$ value of 0.984 (close to 1.0). CAP: Cellulose acetate phthalate

**Table 16: *In vitro* drug release parameters for 24% cellulose acetate phthalate**

| Time (h) | %CDR | Log %CDR | Cube root of % drug remaining | Log % cumulative drug remaining | Square root time | Log time |
|---|---|---|---|---|---|---|
| 0.5 | 0.3 | 0.5228 | 4.63695 | 1.99869 | 0.7071 | −0.3010 |
| 1.0 | 1.8 | 0.2552 | 4.61357 | 1.99211 | 1.00 | 0.00 |
| 1.5 | 18.2 | 1.2600 | 4.34094 | 1.91275 | 1.2247 | 0.1760 |
| 2.0 | 39.2 | 1.5932 | 3.93219 | 1.78390 | 1.4142 | 0.3010 |
| 2.5 | 50.5 | 1.7032 | 3.67171 | 1.69460 | 1.5811 | 0.3979 |
| 3.0 | 58.7 | 1.7686 | 3.45660 | 1.61595 | 1.7320 | 0.4771 |
| 3.5 | 67.3 | 1.8280 | 3.19778 | 1.51454 | 1.8708 | 0.5440 |
| 4.0 | 78.8 | 1.8965 | 2.76765 | 1.32633 | 2.00 | 0.6020 |

CDR: Cumulative drug release

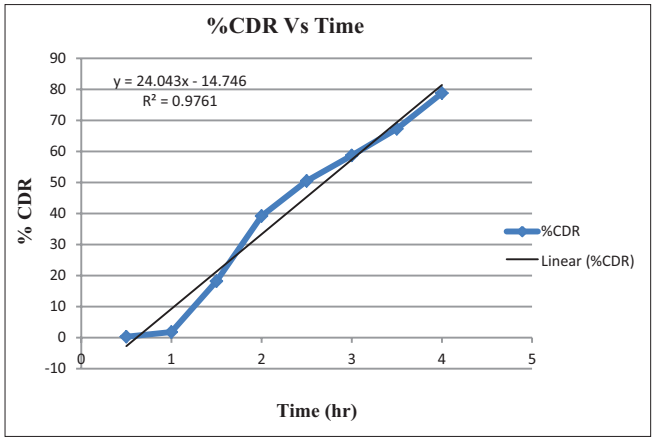


**Figure 27:** Senna release kinetic of 24% cellulose acetate phthalate according to zero-order kinetic

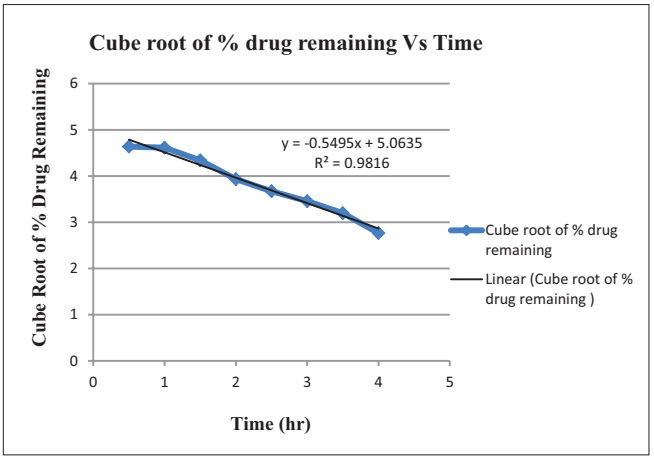


**Figure 29:** Senna release kinetic of 24% cellulose acetate phthalate according to Hixon-Crowell kinetic

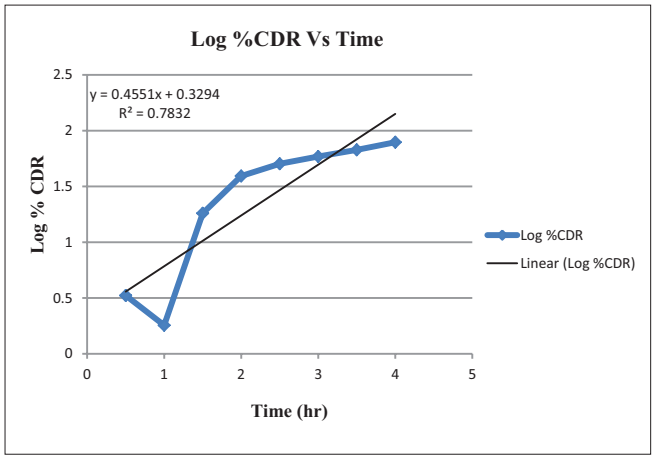


**Figure 28:** Senna release kinetic of 24% cellulose acetate phthalate according to first order kinetic

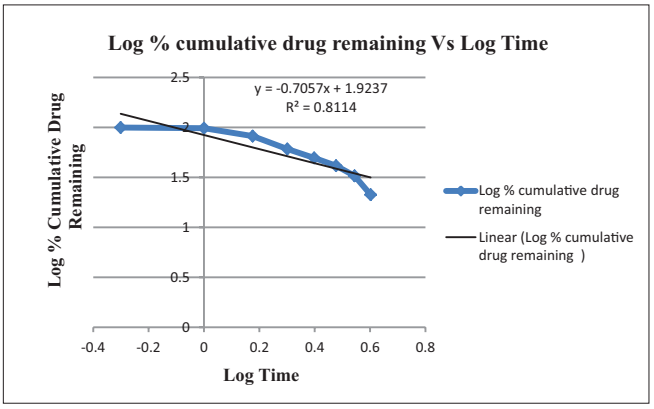


**Figure 30:** Senna release kinetic of 24% cellulose acetate phthalate according to Korsmeyer-Peppas kinetic

**Table 17: Statistical kinetics value for batch 24% CAP**

| Kinetic models | $R^2$ | Slope |
|---|---|---|
| Zero order | 0.976 | 24.04 |
| First order | 0.783 | 0.455 |
| Hixon-Crowell | 0.981 | −0.549 |
| Korsmeyer-Peppas | 0.811 | 0.705 |
| Higuchi kinetic | 0.964 | 66.88 |

Among the entire kinetics model studied for batch having 24% CAP, it was observed that the batch followed Hixon-Crowell kinetic model because of having maximum $R^2$ value of 0.981 (close to 1.0). CAP: Cellulose acetate phthalate

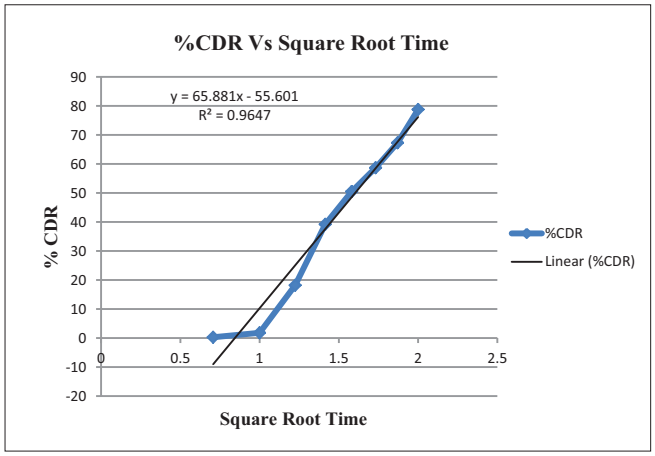


**Figure 31:** Senna release kinetic of 24% cellulose acetate phthalate according to Higuchi kinetic

*In vitro* drug release parameters for 24% CAP [Table 16 and Figures 27-31].

The statistical kinetics values of batch having 24% CAP [Table 17].

## SUMMARY

The entire kinetic models studied for all the batches of different concentration of CAP. The batch containing 4% CAP, it was observed that the batch followed Zero order kinetic model because of having maximum $R^2$ value of 0.990. The batch having 8% CAP and it was observed that the batch followed Zero order kinetic model because of having maximum $R^2$ value of 0.959. The batch having 12% CAP and it was observed that the batch followed Higuchi model because of having maximum $R^2$ value of 0.999. The batch having 16% CAP and it was observed that the batch followed Hixon-Crowell model and Higuchi model both because of having maximum $R^2$ value of 0.991. The batch having 20% CAP, it was observed that the batch followed zero order kinetic and Higuchi kinetic model because of having maximum $R^2$ value of 0.984. The batch having 24% CAP, it was observed that the batch followed Hixon-Crowell kinetic model because of having maximum $R^2$ value of 0.981.

## CONCLUSION

The entire kinetic studies of all the batches having of different percentage age of CAP revealed that enteric coated formulation of senna having 12% CAP have good results and formulation follow Higuchi kinetic model because of having maximum $R^2$ value of 0.999.

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