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Research Article

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DISSOLUTION ENHANCEMENT OF IBUPROFEN USING SURFACTANTS

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ABSTRACT

Ibuprofen is highly water in-soluble drug. An attempt was taken to study the effect of PEG by using solid solution method. In this experiment Cremophor RH 40 and Cremophor EL was used as solubilizing agent. Capsules were prepared manually and drug release was studied using USP basket method at 50 rpm and controlling the temperature 37^0C. Distilled water was used as dissolution medium. The amount of drug release was measured form the absorbance of UV spectrophotometer at 264nm. The release of drug was plotted in Higuchi release pattern, zero and first order release pattern. This study showed that Cremophor RH 40 and Cremophor EL have effect the release profile of capsule ibuprofen. From this work it was found that it is possible to increase the release of ibuprofen by using Cremophor RH 40 and Cremophor EL.

KEYWORDS: PEG (Poly Ethylene Glycol), Surfactants.

1. INTRODUCTION

Ibuprofen is a non-steroidal anti-inflammatory drug commonly used to reduce fever, pain and stiffness. It works by inhibiting the production of prostaglandins. The process of dissolution plays a vital role in liberation of a drug from its dosage from and making it available for subsequent gastrointestinal absorption. The study is designed to evaluate the effect of solubilizing agent on the release pattern of drug. Here ibuprofen was used as a model drug. The performance of the dosage form was evaluated in terms of in vitro drug dissolution profile. However, in vitro dissolution tests now-a-days considered to be more advantageous because it is the only test which can more or less indirectly correlate the in-vivo bioavailability. The aim of this study was to investigate, at a molecular level, the structural and dynamic properties of ibuprofen and their solid dispersions with Cremophor EL and Cremophor RH40, which may affect the release properties of these drugs in their dispersed forms. Conventional release capsules dosage form were prepared and then incorporated into two size capsule shell. Effects of different solubilizing agent were assayed by in vitro drug dissolution studies.

2. MATERIALS AND METHODS

2.1 Materials: Ibuprofen was obtained from Xamim, China. Polyethylene Glycol (6000), Cremophor EL, Cremophor RH-40 gift samples were received from BASF, Germany. Potassium di-hydrogen orthophosphate was received from Qualikems Fine Chemicals, India; Sodium hydroxide was received from Merck Specialties Private Limited, India.

2.2 Preparation of capsule

Active drug was taken into a vial. Then the excipients were added one by one with it. Vial along with ingredients was melted with the help of liquid paraffin oil. Then the mixture was stirred in one direction with the help of glass rod. Then the melted mixture was made into solid lump. The solid lump was converted into powder form with the help of mortar and pestle. Then the power particles were passed sieve in mesh size 40.

50 mg Equivalent weight of ibuprofen were taken in each 0 size capsule shell and filled the capsule carefully. Finally the capsules were sealed.

2.3 Formulation of ibuprofen capsule

Table-1:

Item	IB-P- 20%	IB-P- 40%	IB-P- 60%	IB-P- 80%
Ibuprofen	4 gm	3 gm	2gm	1gm
PEG 6000	1gm	2gm	3gm	4gm

Table-2:

Item	IB-P40-RH-0.2	IB-P40-RH-0.4	IB-P40-RH-0.6	IB-P40-RH-0.8	IB-P40-RH-1.0
Ibuprofen	3 gm	3 gm	3gm	3gm	3gm
PEG 6000	1.9 gm	1.8 gm	1.7gm	1.6 gm	1.5 gm
Cremophor- RH40	100 mg	200 mg	300 mg	400 mg	500 mg

Table-3:

Item	IB-P40-EL-0.2	IB-P40-EL -0.4	IB-P40-EL-0.6	IB-P40- EL -0.8	IB-P40- EL -1.0
Ibuprofen	3 gm	3 gm	3gm	3gm	3gm
PEG 6000	1.9 gm	1.8 gm	1.7gm	1.6 gm	1.5 gm
Cremophor EL	100 mg	200 mg	300 mg	400 mg	500 mg

2.4 Standard curve of ibuprofen

100mg of ibuprofen powder was accurately weighted and dissolved with 100ml phosphate buffer (pH-7.2) in a 100ml volumetric flask. 10ml from that solution was taken into another 100ml volumetric flask and again made the total volume of that solution 100ml by adding desired amount of phosphate buffer (pH-7.2). These solutions were then analyzed by UV spectrophotometer and absorbance of different concentrations (0, 10, 15, 20, 25, 30, 40, 60, 80, 100µg/lit) were taken at 264nm and absorbance was noted. Absorbance values were then put against respective concentration and standard curve of Ibuprofen was produced.

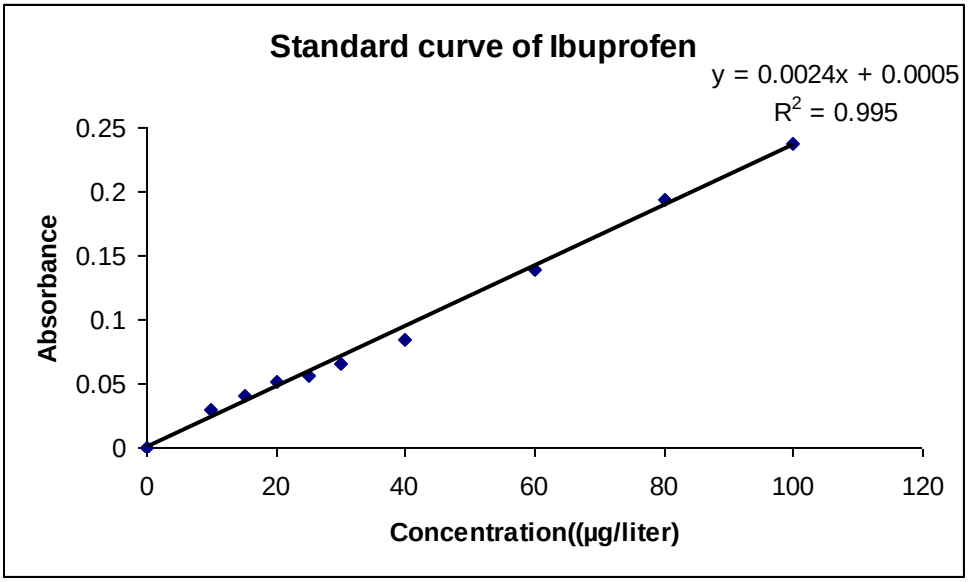

Figure: Standard Curve of Ibuprofen.

2.5 Preparation of Phosphate buffer pH-7.2

For 1 liter, 13.61 gm of potassium dihydrogen ortho-phosphate was taken in a 500ml volumetric flask and 4gm of sodium hydroxide (NaOH) was taken in another 500ml of volumetric flask. They were dissolved and adjusted the pH-7.2.

2.6 Dissolution of Ibuprofen capsule

The dissolution studies were carried out using a "USP Type III Dissolution Apparatus'. One liter of distilled water was used as a dissolution medium. One capsule was placed into each of one basket; these were inserted in the vessels. The baskets were rotated at 50 rpm. The temperature of the dissolution medium set at 37 ^{0}C. 5ml of sample solution was withdrawn from each vessel at predetermined intervals for assay of drug content and was replaced by a fresh portion of medium. Drug content of the sample solution i.e. quantity of drug released, was determined by spectrophotometirc analysis using "SHIMADZU UV Spectrophotometer''. Maximum absorbance for ibuprofen is taken at about 264 nm. Distilled water was used as a blank solution. The average value of released drug was used for data analysis.

2.7 Determination of melting point

Certain amount of water was taken into water-bath and heated for obtaining a desired temperature. A beaker with certain amount of paraffin was placed into that water-bath. Each capillary tube was slightly filled with each formulation and that capillary tube was put in contact with a thermometer. Then this thermometer along with this capillary tube was placed into that heated water-bath and when the formulation was started to melt and completely melted note that value. Actually this

value- range was the melting point of that particular formulation.

Melting point of all formulation

The melting point of the formulation

Formulation	Melting Point(^{0}C)
IB-P20%	60-71
IB-P40%	45-60
IB-P60%	38-46
IB-P80%	46-52
IB-P40-RH40-0.2	44-64
IB-P40-RH40-0.4	21-59
IB-P40-RH40-0.6	43-64
IB-P40-RH40-0.8	38-61
IB-P40-RH40-1.0	37-62
IB-P40-EL-0.2	48-63
IB-P40-EL-0.4	41-63
IB-P40-EL-0.6	38-58
IB-P40-EL-0.8	38-57
IB-P40-EL-1.0	38-62

3. RESULT AND DISCUSSION

Ibuprofen was a poorly soluble drug. It was made soluble and brought into the dissolution first by the addition of surfactant such as (Tween-80, 60; SLS; Span-20, 80; Cremophore –EL, RH40; & ethanol) using highly alkaline media 0.1M NaoH at pH 11.2.

Drug release kinetics was done by basket method using distilled water as dissolution medium at room temperature (37^{0}C) at 50 rpm speed. The sample was collected for 3 hour studies and percentage of drug release at different time interval was calculated from the UV absorbance reading. 5ml syringe was used to take 5ml sample from each sample basket and 5ml fresh distilled water was added after the sample was taken into each sample basket. Sample was filtered and % release of ibuprofen was calculated from UV absorbance reading of sample. As two sample capsules were taken from each formulation average % release of drug was calculated for each formulation.

The formulation IB-P-20%; IB-P-40%; IB-P-60%; IB-P-80%, IB-P40-RH40-0.2, IB-P40-RH40-0.4, IB-P40-RH40-0.6, IB-P40-RH40-0.8, IB-P40-RH40-1.0, IB-P40-EL-0.2, IB-P40-EL-0.4, IB-P40-EL-0.6, IB-P40-EL-0.8, IB-P40-EL-1.0 showed about 98.28%, 98.28%, 99.48%, 99.48%, 98.28%, 98.88%, 98.88%, 98.28%, 99.48%, 96.48%, 98.28%, 98.28%, 98.28%, 98.28% release respectively within 3hours. The release was plotted in three different models, via, Zero order, Higuchi and First order respectively.

The correlation coefficients values of the trend lines of the graphs showed that formulation IB-P-20%, IB-P-40%, IB-P-60%, IB-P-80%, IB-P40-RH40-0.2, IB-P40-RH40-0.4, IB-P-40-RH40-0.6, IB-P40-RH40-0.8, IB-P40-RH40-1.0, IB-P40-EL-0.2, IB-P40-EL-0.4, IB-P40-EL-0.6, IB-P40-EL-0.8, IB-P40-EL-1.0 show best fits in Higuchian pattern.

3.1 Correlation coefficient (R^2) value of all formulation

Formulation	Zero order plot	First order plot	Higuchi plot
IB-P-20%	0.9169	0.2962	0.9182
IB-P-40%	0.9169	0.3345	0.917
IB-P-60%	0.9169	0.4165	0.9176
IB-P-80%	0.9169	0.4282	0.9185
IB-P40-RH40-0.2	0.9169	0.2681	0.9281
IB-P40-RH40-0.4	0.9169	0.3186	0.9267
IB-P40-RH40-0.6	0.9169	0.3026	0.9242
IB-P40-RH40-0.8	0.9169	0.239	0.9202
IB-P40-RH40-1.0	0.9169	0.3361	0.9865
IB-P40-EL-0.2	0.9169	0.1615	0.9753
IB-P40-EL-0.4	0.9169	0.3265	0.928
IB-P40-EL-0.6	0.9169	0.2261	0.9727
IB-P40-EL-0.8	0.9169	0.303	0.9206
IB-P40-EL-1.0	0.9169	0.2963	0.9722

3.2 Drug release profile of IB-P20%

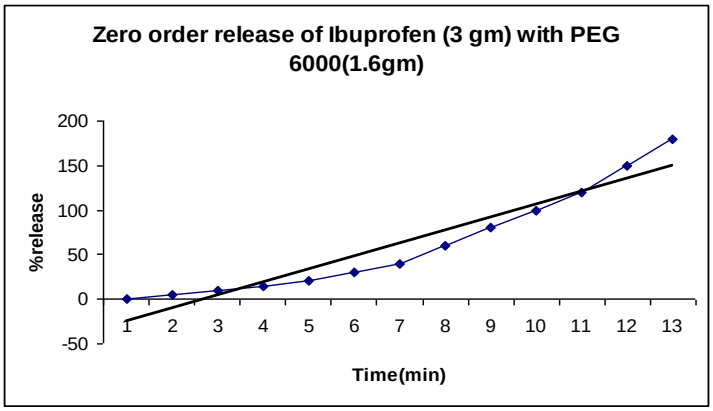

Fig 1: Zero order release of Ibuprofen (3 gm) with PEG 6000(1.6gm).

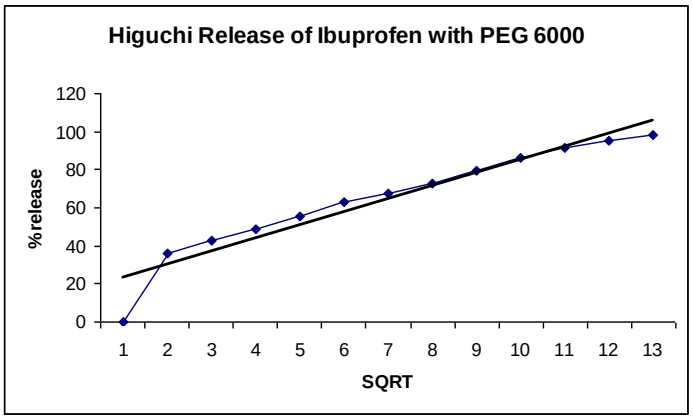

Fig 2: Higuchi Release of Ibuprofen with PEG 6000.

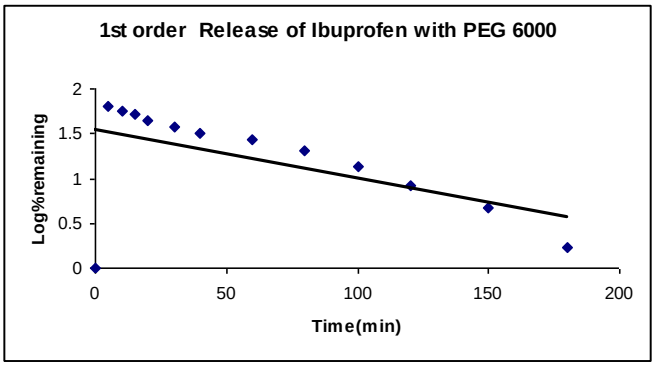

Fig 3: 1st order Release of Ibuprofen with PEG 6000.

3.3 Drug release profile of IB-P40%

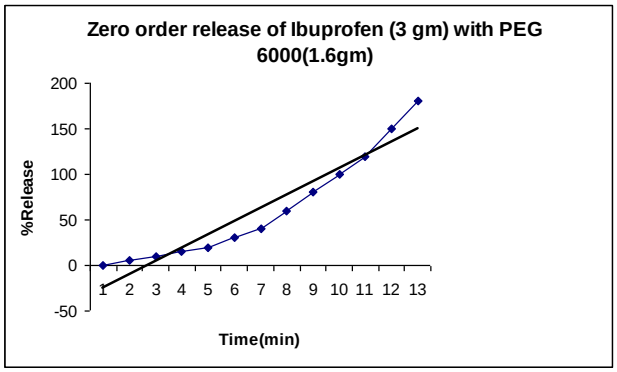

Fig 4: Zero order release of Ibuprofen (3 gm) with PEG 6000(1.6gm).

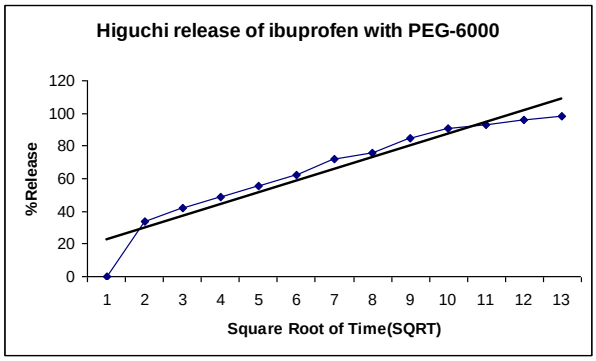

Fig 5: Higuchi Release of Ibuprofen with PEG 6000.

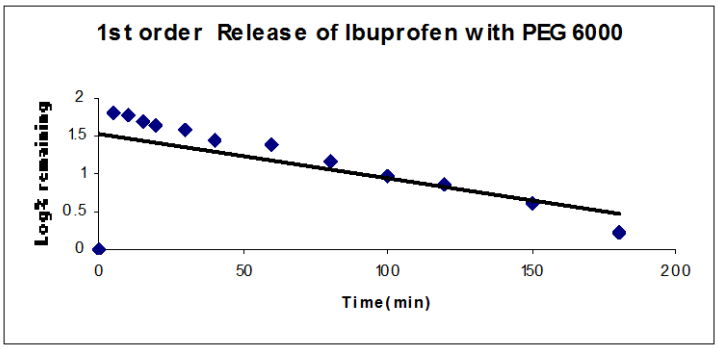

Fig 6: 1st order Release of Ibuprofen with PEG 6000.

3.4 Drug release profile of IB-P60%

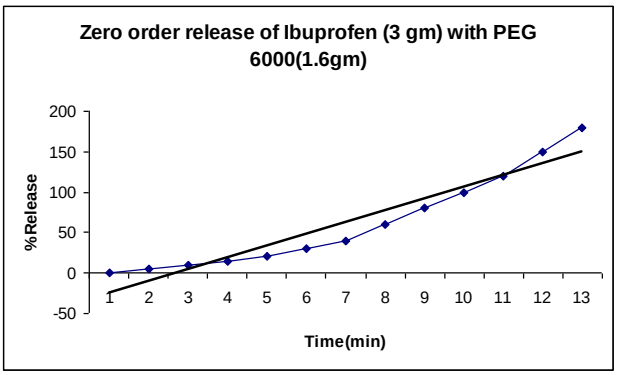

Fig 7: Zero order release of Ibuprofen (3 gm) with PEG 6000(1.6gm).

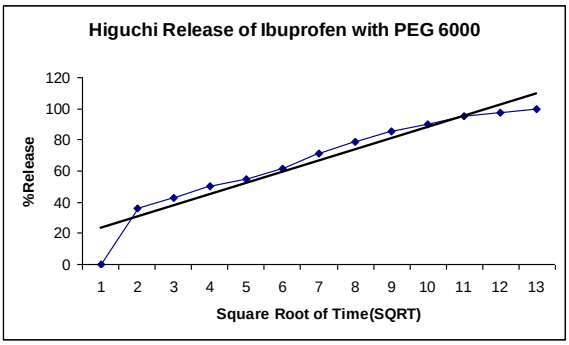

Fig 8: Higuchi Release of Ibuprofen with PEG 6000.

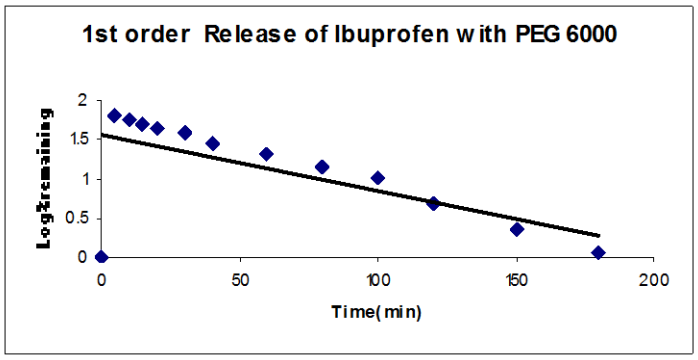

Fig 9: 1st order Release of Ibuprofen with PEG 6000.

3.5 Drug release profile of IB-P80%

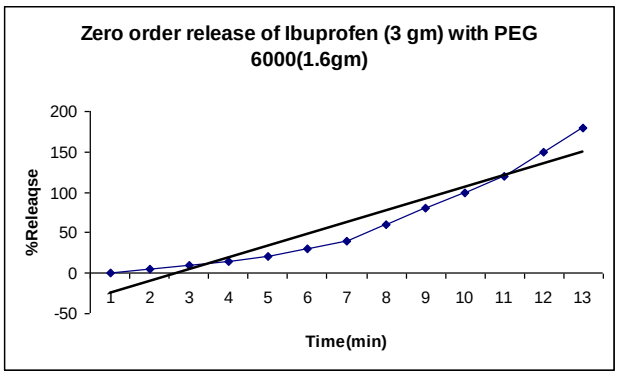

Fig 10: Zero order release of Ibuprofen (3 gm) with PEG 6000(1.6gm).

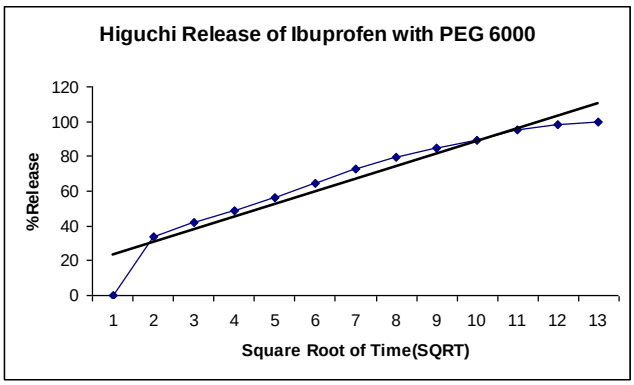

Fig 11: Higuchi Release of Ibuprofen with PEG 6000.

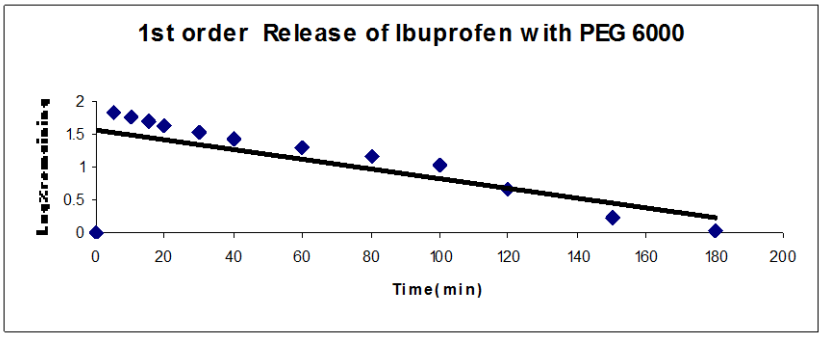

Fig 12: 1st order Release of Ibuprofen with PEG 6000.

3.6 Drug release profile of IB-P40-EL-O.2

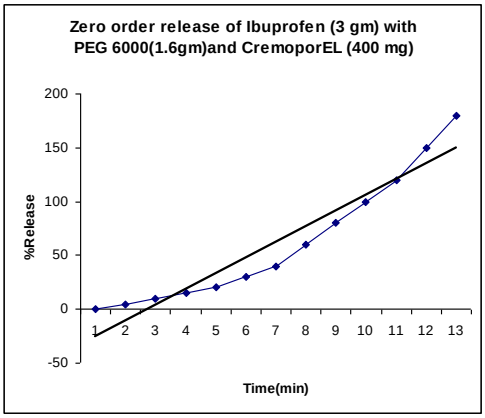

Fig 13: Zero order release of Ibuprofen (3 gm) with PEG 6000(1.6gm) and CremoporEL (400 mg).

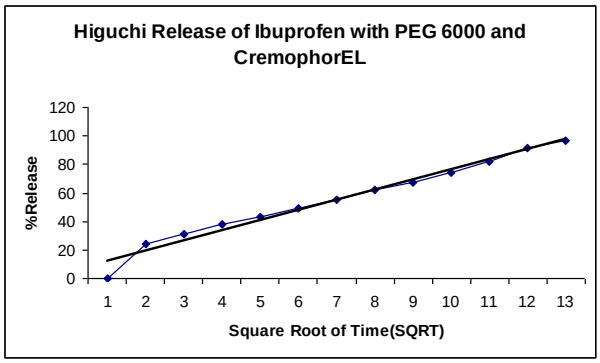

Fig 14: Higuchi Release of Ibuprofen with PEG 6000 and Cremophor EL.

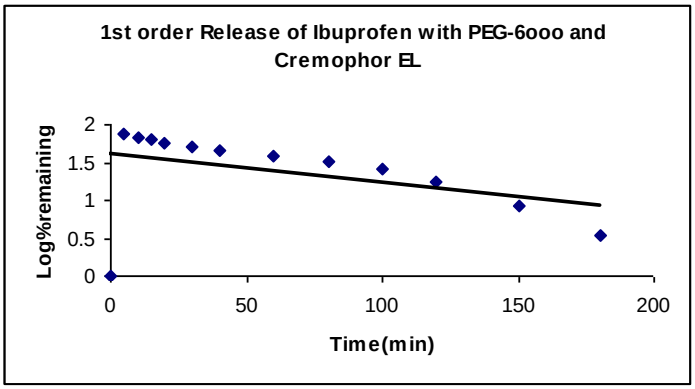

Fig 15: 1st order Release of Ibuprofen with PEG-6ooo and Cremophor EL.

3.7 Drug release profile of IB-P40-EL-O.4

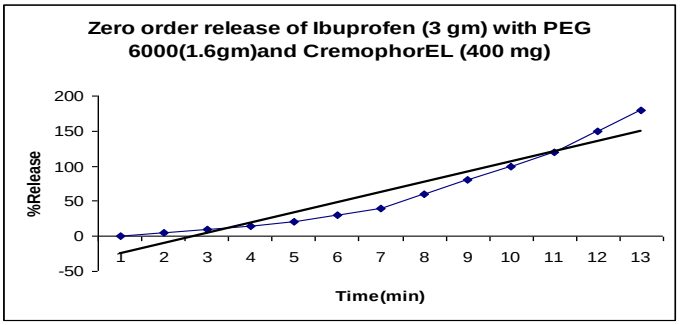

Fig 16: Zero order release of Ibuprofen (3 gm) with PEG 6000(1.6gm) and CremoporEL (400 mg).

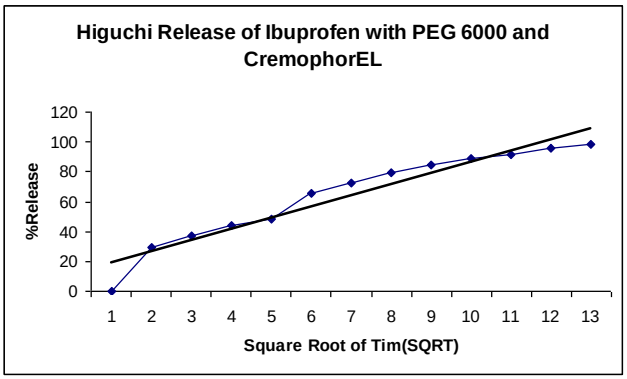

Fig 17: Higuchi Release of Ibuprofen with PEG 6000 and Cremophor EL.

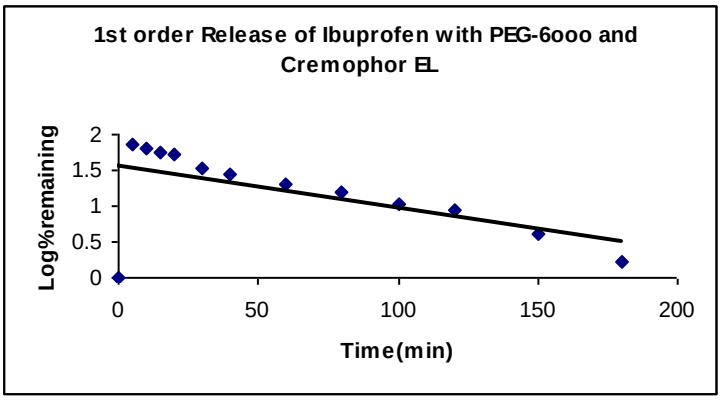

Fig 18: 1st order Release of Ibuprofen with PEG-6ooo and Cremophor EL.

3.8 Drug release profile of IB-P40-EL-O.6

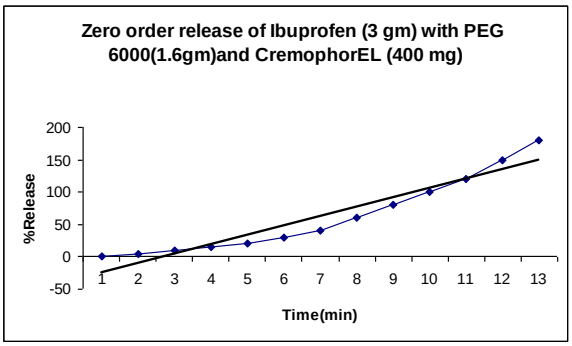

Fig 19: Zero order release of Ibuprofen (3 gm) with PEG 6000(1.6gm) and Cremopor EL (400 mg).

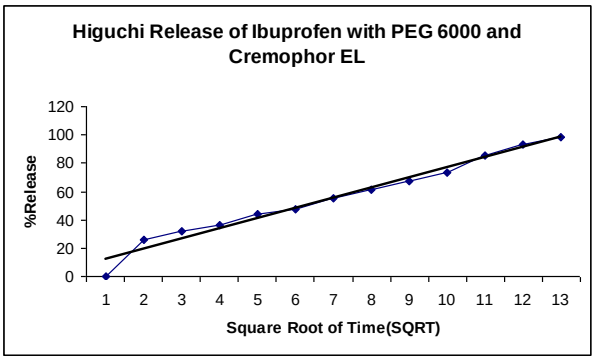

Fig 20: Higuchi Release of Ibuprofen with PEG 6000 and Cremophor EL.

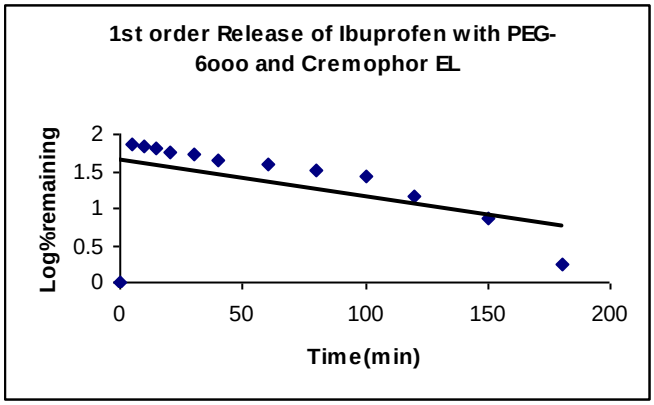

Fig 21: 1st order Release of Ibuprofen with PEG-6ooo and Cremophor EL.

3.9 Drug release profile of IB-P40-EL-O.8

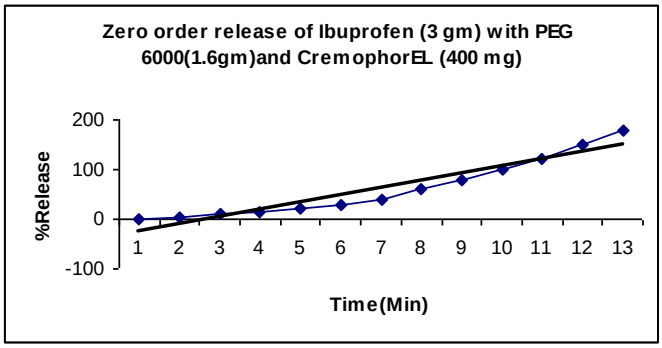

Fig 22: Zero order release of Ibuprofen (3 gm) with PEG 6000(1.6gm) and Cremophor EL (400 mg).

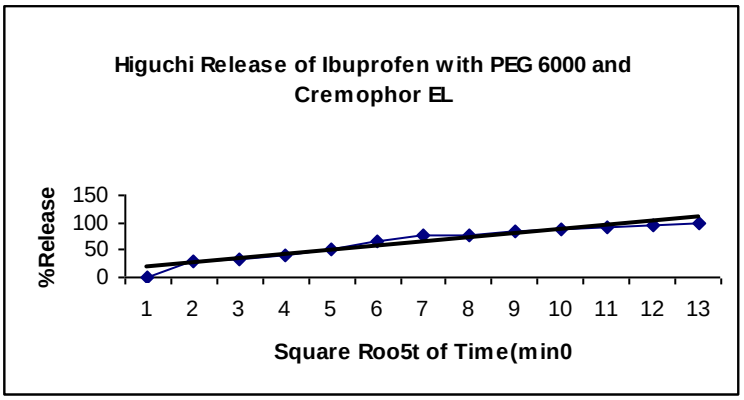

Fig 23: Higuchi Release of Ibuprofen with PEG 6000 and Cremophor EL.

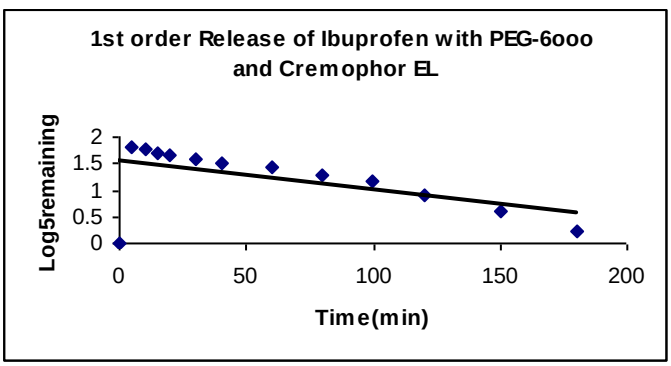

Fig 24: 1st order Release of Ibuprofen with PEG-6ooo and Cremophor EL.

3.10 Drug release profile of IB-P40-EL-1.0

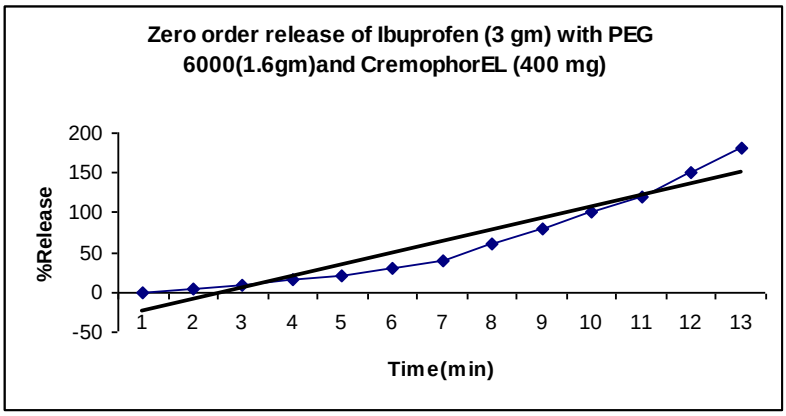

Fig 25: Zero order release of Ibuprofen (3 gm) with PEG 6000(1.6gm) and Cremophor EL (400 mg).

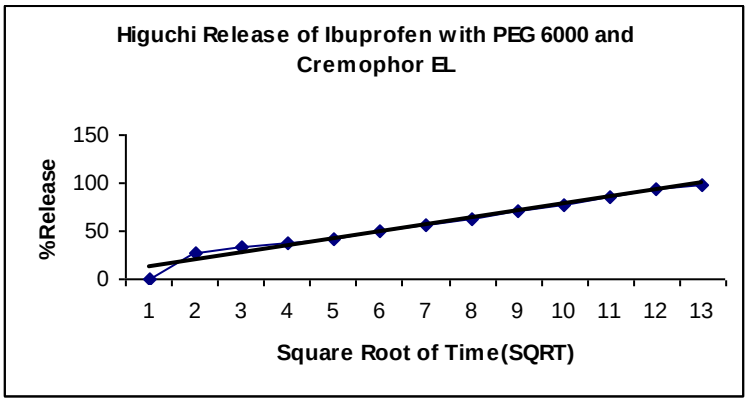

Fig 26: Higuchi Release of Ibuprofen with PEG 6000 and Cremophor EL.

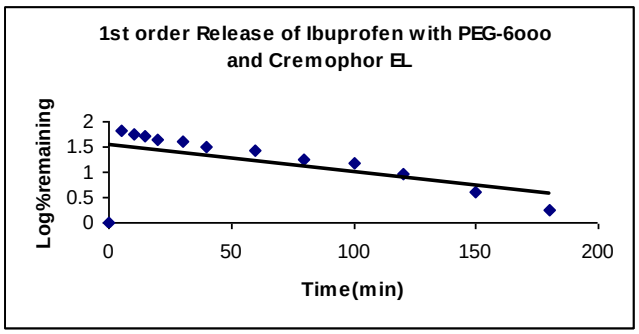

Fig 27: 1st order Release of Ibuprofen with PEG-6ooo and Cremophor EL.

3.11 Drug release profile of IB-P40-RH40-O.2

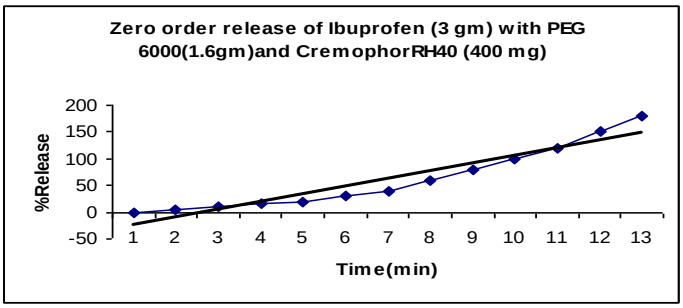

Fig 28: Zero order release of Ibuprofen (3 gm) with PEG 6000(1.6gm) and CremophorRH40 (400 mg).

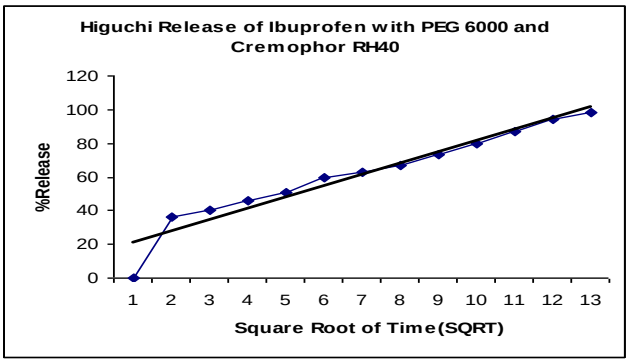

Fig 29: Higuchi Release of Ibuprofen with PEG 6000 and Cremophor RH40.

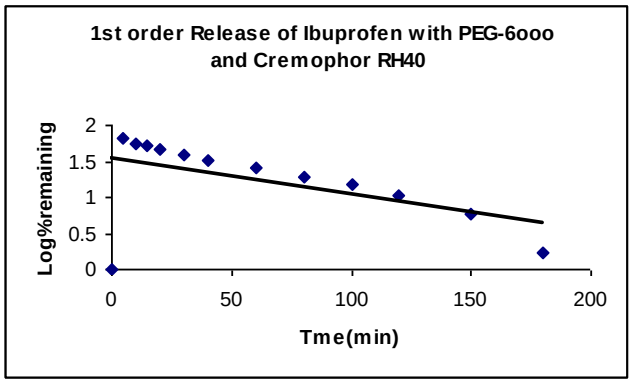

Fig 30: 1st order Release of Ibuprofen with PEG-6ooo and Cremophor RH40.

3.12 Drug release profile of IB-P40-RH40-O.4

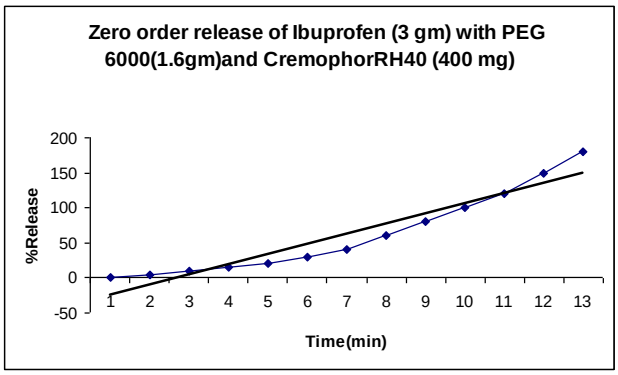

Fig 31: Zero order release of Ibuprofen (3 gm) with PEG 6000(1.6gm) and CremophorRH40 (400 mg).

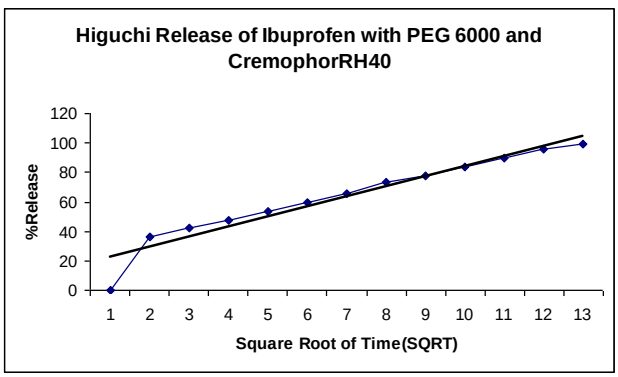

Fig 32: Higuchi Release of Ibuprofen with PEG 6000 and Cremophor RH40.

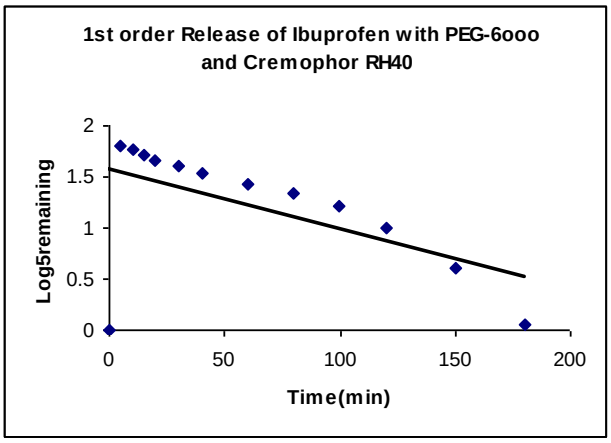

Fig 33: 1st order Release of Ibuprofen with PEG-6ooo and Cremophor RH40.

3.13 Drug release profile of IB-P40-RH40-O.6

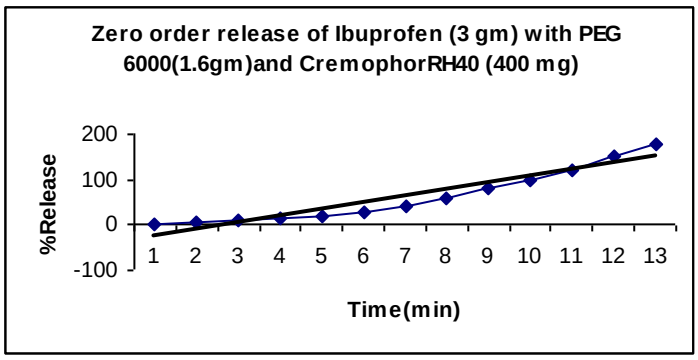

Fig 34: Zero order release of Ibuprofen (3 gm) with PEG 6000(1.6gm) and CremophorRH40 (400 mg)

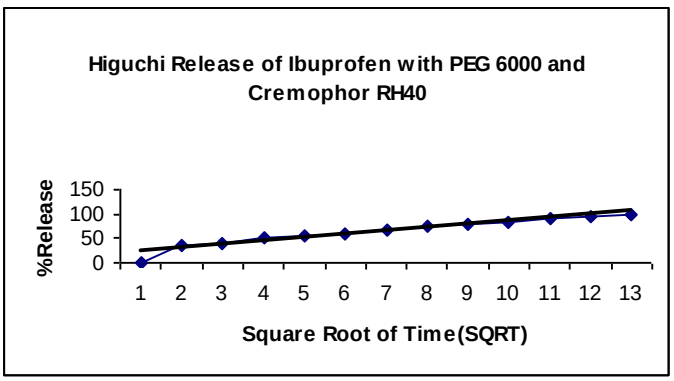

Fig 35: Higuchi Release of Ibuprofen with PEG 6000 and Cremophor RH40.

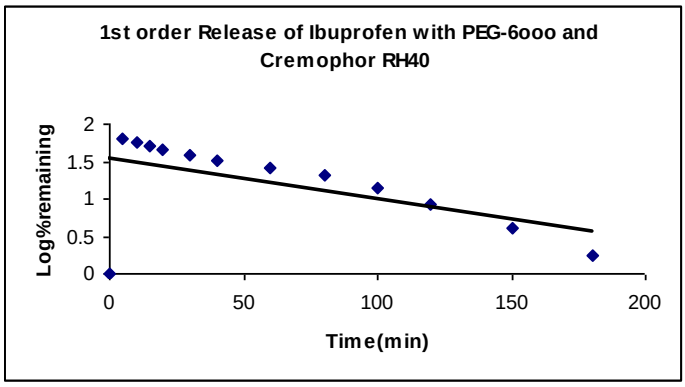

Fig 36: 1st order Release of Ibuprofen with PEG-6ooo and Cremophor RH40.

3.14 Drug release profile of IB-P40-RH40-O.8

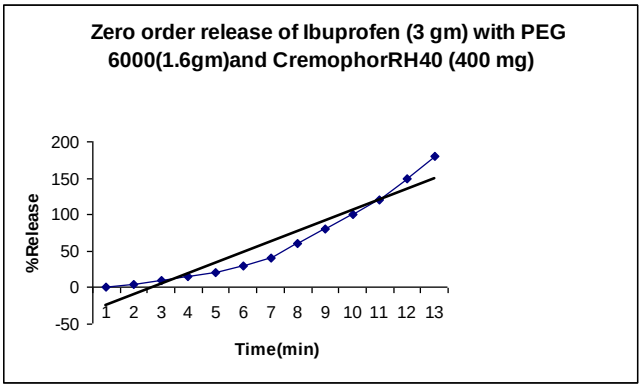

Fig 37: Zero order release of Ibuprofen (3 gm) with PEG 6000(1.6gm) and CremophorRH40 (400 mg).

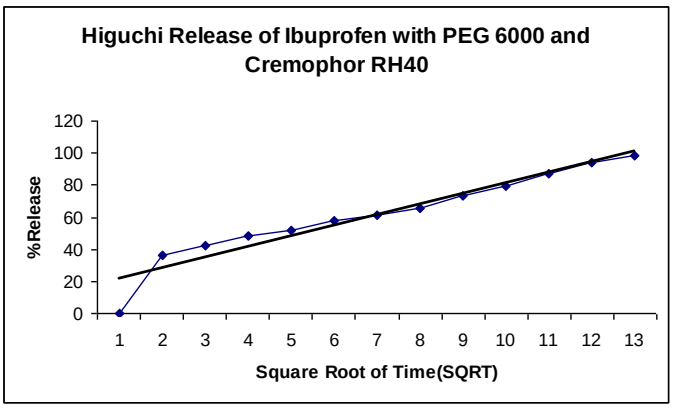

Fig 38: Higuchi Release of Ibuprofen with PEG 6000 and Cremophor RH40.

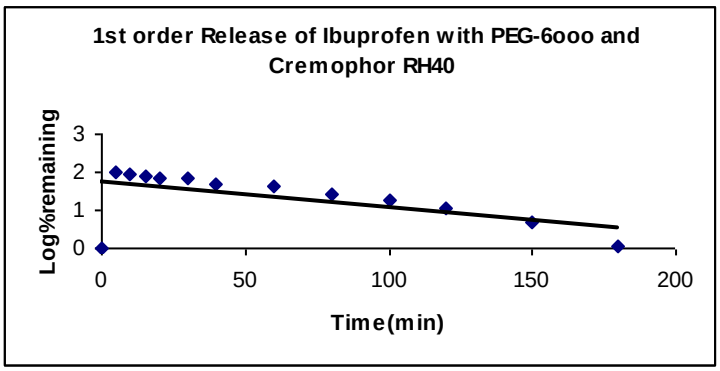

Fig 39: 1st order Release of Ibuprofen with PEG-6ooo and Cremophor RH40.

3.15 Drug release profile of IB-P40-RH40-1.0

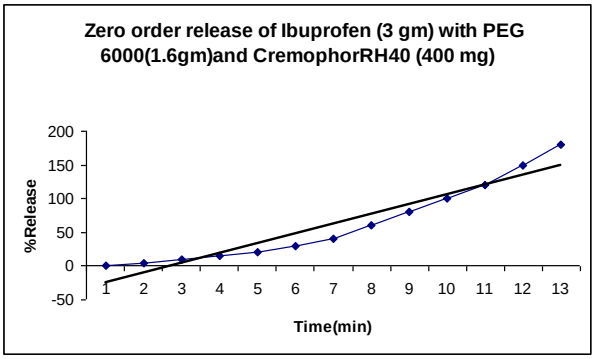

Fig 40: Zero order release of Ibuprofen (3 gm) with PEG 6000(1.6gm) and CremophorRH40 (400 mg).

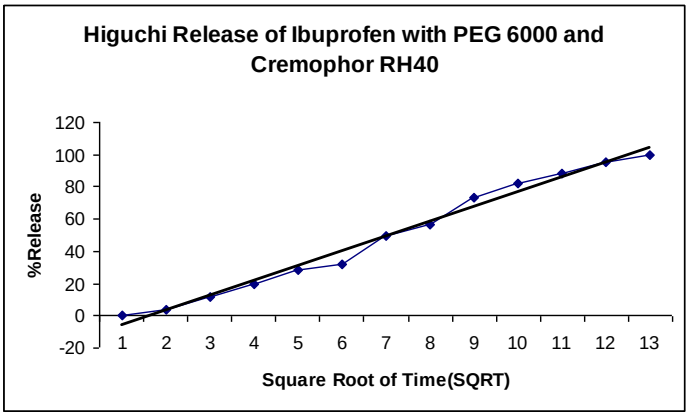

Fig 41: Higuchi Release of Ibuprofen with PEG 6000 and Cremophor RH40.

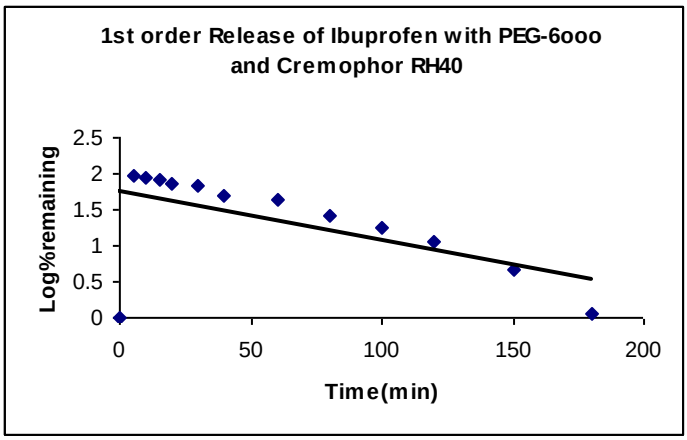

Fig 42: 1st order Release of Ibuprofen with PEG-6ooo and Cremophor RH40.

4.0 CONCLUSION

Ibuprofen is poorly water soluble drug and it does not soluble in the water easily. In this experiment different surfactant has been used along with the drug (Ibuprofen). Here different surfactant (CremophorRH40; Cremophor EL) which has been used act as carrier and does effect on the solubility of ibuprofen. As a result the dissolution curve follows the Higuchian pattern. This similarity of the curve indicates that the solubility of poorly water soluble drug increases by the use of such kind of surfactant.

5.0 REFERENCES

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