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DESIGN, CHARECTERIZATION AND *IN-VITRO, IN-VIVO* CORRELATION STUDIES FOR ELETRIPTAN LOADED TRANSDERMAL PATCHES

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ABSTRACT

Eletriptan is a 5-HT1D (5-hydroxy tryptamine 1D)-receptor agonist, used in the treatment of migraine and cluster headache. Eletriptan has been shown to have a low oral bioavailability in human volunteers (50%) because of high first pass metabolism. The present investigation is to formulate matrix type transdermal drug delivery system which is loaded with Eletriptan using Hydroxy Propyl methyl cellulose k-4 and k-15 individually as a release controlling polymers, Propylene glycol as permeation enhancer and Dibutylpthalate as a plasticizer. The prepared patches were characterized by diffusion studies with Franz diffusion cell and further correlated with animal studies. The work was aimed to develop the TDDS which controls the release of Eletriptan for 48 hrs. The models used were zero and first-order equations, Higuchi and Korsmeyer-Peppas models. Based on physicochemical properties and in vitro release studies, patch containing Hydroxy propyl methyl cellulose k15(500mg) emerged as a best formulation. Skin irritation studies for the transdermal patches were assessed and were found to be free of irritation.

Key words: Eletriptan, Migraine, transdermal formulation, kinetic models

INTRODUCTION

Oral drug delivery is the most desirable route for drug administration whenever systemic effects are intended. But low oral bioavailability of some compounds have prompted the search of more effective routes for their systemic delivery. Subcutaneous administration is an alternative; however, dislike of injections or inability to self-administer by this route makes subcutaneous treatment unacceptable to some individuals. The dissolution rate of poorly water soluble drugs often becomes a rate-limiting step in their absorption from the GI tract. Many techniques have been developed to enhance the absorption of poorly water soluble practically water insoluble drugs. Most of them increase surface area of drugs to improve solubilization behaviour. If a drug candidate has reasonable member in permeability then often the rate limiting process of absorption is the drug dissolution step. This is the charecterstic of compounds that can be categorized as biopharmaceutical classification system (BCS Class-II) formulations play a major role in determining the rate and extent of absorption of such drugs from the gastrointestinal tract, when water solubility is less than 1 mcg per ml, then the bioavailability from the conventional tablet formulation may be unacceptable.

A recent approach to drug delivery is to deliver the drug into systemic circulation at predetermined rate using skin as a site of application. Transdermal delivery has many advantages over conventional modes of drug administration, it avoids hepatic first pass metabolism, potentially decreases side effects and improves patient compliance. Drug delivery with transdermal patch systems exhibit slow, controlled drug release and absorption. The plasma drug concentration does not vary significantly over time. Transdermal delivery system is a growing market that is expected to expand in the near future with the discovery of new drug treatment applications and technologies. These all above things justify a need of Transdermal drug delivery.

Migraine is a chronic neurologic disorder with heterogeneous characteristics resulting in a range of symptom profiles like burden, and disability. Current

management of migraine deals with Triptans. This drugs used in migraine or during attack. EletriptanHBr is a 5-HT1D (5-hydroxy tryptamine 1D)-receptor agonist, used in the treatment of migraine and cluster headache. EletriptanHBr has been shown to have a low oral bioavailability in human volunteers (50%) because of high first pass metabolism.The potential advantages of Eletriptan lie firstly in its lipophilicity reflected as an increased rate of absorption and Tmax compared to sumatriptan. This is manifested in a modest advantage over sumatriptan in terms of speed of onset, 2 h headache response and 2 h pain free.

MATERIALS AND METHODS

Materials: Eletriptan purchased from Mylan Lab. ltd, Hydroxy propylmethylcellulose obtained from Shreeji chemicals, Dimethylformamide, Propyleneglycol obtained from Loba Chemie, Dibutylphthalate, Potassium dihydrogenphosphate, Sodiumhydroxide, Dimethylsulfoxide, Glycerine, Carbopol934, Eudragit RS100 obtained from S.D. Fine Chem. Ltd, All other ingredients, reagents and solvents were of analytical grade.

Methods: Transdermal patches of Eletriptan were prepared by using polymers HPMC k-4 and k-15 by solvent evaporation technique for the formulations shown in Table 5.3. A solution is prepared by dissolving weighed amount of drug and polymer separately in water. To the mixture Dibutylpthalate,propylene glycol were added and mixed by using magnetic stirrer until a homogenous solution is formed. The drug-polymer solution is casted in a bangle of area 16cm^2 which is placed in a petridish. The mould was kept aside for drying at room temperature for 24 hrs. Inverted funnel was placed over the mould to prevent the current of air. After drying, the patches were peeled from petridish, and preserved in desiccators for further studies.

EVALUATION PARAMETERS

Physical appearance: The prepared patches were physically examined for colour, clarity and surface texture.

Thickness uniformity: The thickness of patches was measured by using electronic caliper, with a least count-0.01mm. Thickness was measured at 3different points on the film and average readings were taken.

Uniformity of weight: The patch of size 1x1 cm^2 was cut and weight of each patch was taken individually, the average weight of the patch was calculated.

Tensile strength: Tensile strength of the patches was determined with Universal Strength Testing Machine. The film was fixed between these cell grips and force was gradually applied till the film broke.

Tensile strength = Tensile Load at break / Cross sectional area

Folding endurance: The folding endurance was measured manually for the prepared patches. A strip of patch (2xcm^2) was cut and repeatedly folded at the same place till it broke. The number of times the film could be folded at the same place without breaking gave the value of folding endurance.

Percentage moisture loss: The patches were weighed individually and kept in a dessicator containing calcium chloride. The final weight was noted when there was no change in the weight of individual patch. The percentage of moisture content was calculated.

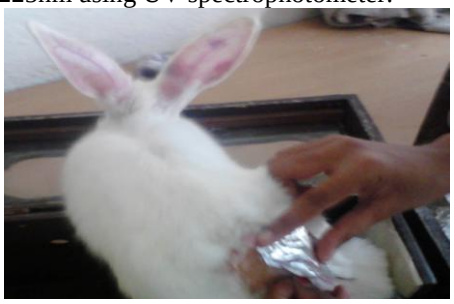
Percentage moisture uptake: The patches were weighed accurately and placed in a dessicator where a humidity condition of 80-90% RH was maintained by using saturated solution of potassium chloride. The patches were kept until uniform weight is obtained, then taken out and weighed.

Drug content uniformity: The patches were tested for the content uniformity. The patches of size 1 cm^2 was cut and placed in a 100 ml volumetric flask. The contents were stirred using a magnetic bead for 24 hrs to dissolve the patches. Subsequent dilutions were made with phosphate buffer (pH 7.4). The absorbance of the solution was measured against the corresponding blank solution at 225 nm using UV-visible spectrophotometer.

***In vitro* release studies:** The fabricated patch were cut into 1cm^2 and placed on the semi permeable membrane and attached to diffusion cell, receptor compartment was filled with phosphate buffer solution of pH 7.4 at 37±1^{0}c. The elution medium was stirred magnetically. The aliquots (1ml) was withdrawn at predetermined time intervals and the samples were analysed for drug content using UV spectrophotometer at 225nm.

***In-Vivo* skin irritation studies:** Skin irritation studies were performed on healthy rabbits. The dorsal surface (50 cm^2) of the rabbits was cleaned, and the hair was removed by shaving. The best formulation (F10) was placed over the skin with the use of adhesive tape and was removed after 24 hrs. The resulting skin reaction was evaluated.

***In-Vivo* drug content test:** A set of healthy rabbits were selected, they were checked to ensure that they were free from disease. The dorsal surface of the selected rabbits was cleaned and hair was removed. The dose of Eletriptan was calculated according to the body weight i.e., 1mg. The patch was placed on the dorsal surface, after 48hrs patch was removed and place in a 100 ml volumetric flask with phosphate bufer pH-7.4 and the drug content was analyzed at 225nm using UV spectrophotometer.



***In-Vivo* drug release studies:** Protocols for all animal experiments were approved by CPCSEA. Fours male rabbits of 10–12 weeks old weighing 2–3 kg were selected. They were kept with husk bedding and fed with standard diet and water. Light and dark cycle with 12 h light and 12 h dark was maintained. The temperature, RH conditions were 28±2°C and 60±15% respectively. The dorsal surface of the selected rabbits was cleaned and hair was carefully shaven. Blood samples were collected from the ear vein prior to application of films and then at 1, 2, 4, 6, 10, 23, 24, 28, 32, 36 and 48 h post application. The withdrawn blood samples were stored in well closed tubes under refrigeration (–20 °C) until further analysis. Centrifugation at 5000 rpm is carried for the collected blood sample, from that aqueous layer was separated and amount of drug release is estimated from samples using U.V Spectrophotometer at a wavelength of 225nm.

RESULTS AND DISCUSSION

Analytical Studies: The λmax of Eletriptan in pH 7.4 phosphate buffer solution was found to be 225 nm which is same as that of literature review and it is shown in the table no.1.1, The caliberation curve of Eletriptan in pH 7.4 phosphate buffer solution shows linearity with r^2 of 0.998 shown in fig no.1.1.

Preformulation studies: The following preformulation studies were performed for Eletriptan

Melting point: Melting point of Eletriptan is 169±1.15°C (n = 3). This value is same as that of the literature citation.

Solubility studies: Eletriptan is freely soluble in distilled water (21.4mg/ml), phosphate buffer pH 7.4, methanol, chloroform, acetone and ether.

Partition coefficient: Partition coefficient determination study of Eletriptan was done with n-octanol and water. The logarithmic value of partition coefficient (log pka) of Eletriptan was found to be 10.38. This indicates that Eletriptan is lipophilic in nature.

pH: The pH of freshly prepared 1% aqueous solution of Eletriptan was found to be 3.46,

Drug-Excipient compatibility studies: The characteristic peaks of Eletriptan for IR spectra of Eletriptan, HPMC k-4 and k-15 alone and their combinations were not affected and prominently in table no-1.2.

Preparation of Transdermal patches of Eletriptan. The transdermal patches were successfully prepared for the compositions given in table No-1.4. The prepared patches were stored in aluminum pouch and preserved in desiccators for further studies.

Evaluation of patches

Physical appearance: The patches formed were smooth and transparent/translucent in appearance.

Thickness: With the help of Digital calipers, the thickness of patches was measured and the average thickness was noted. The thickness results are given in table No-1.5. The result indicates that there was no much difference in the thickness within the formulations.

Weight uniformity: Drug loaded patches ($1x1cm^2$) were tested for uniformity of weight and the results of weight uniformity are given in table No- 1.6. Lesser S.D. values indicate that the patches are uniform.

Tensile strength: With increase in HPMC proportion the tensile strength of patches was increased. More the solubility of the polymer higher will be the tensile strength. The results are given in the table No- 1.5.

Folding endurance: The recorded folding endurance of the patches was shown in table No-1.5. It depicits all formulations have good film properties. The results varied with the change in HPMC concentration.

Percentage moisture absorption: The recorded Percentage moisture absorption of the patches was shown in table No- 1.6. The results show the moisture absorption of all the patches are within the acceptable limit.

Percentage moisture loss: The recorded Percentage moisture loss of the patches was shown in table No-1.6. The formulation containing HPMC k-4 alone shows significant loss of moisture when compare to other patches.

Drug content uniformity: Drug content of the patch was carried out to ascertain that the drug is uniformly distributed into the formulation. The results obtained are represented in the table No-1.6. From the results obtained, it was clear that there was proper distribution of Eletriptan in the film formulations. Hence it was concluded that drug was uniformly distributed in all the formulation.

***In-vitro* release studies:** In vitro release studies of Eletriptan patches were carried out in diffusion cell using commercial available semi permeable membrane and phosphate buffer (pH 7.4) as a diffusion medium. The release profile data of Eletriptan were given in table No- 1.7 respectively for patches F1 to F10, Perusal to table No-1.7 From all the formulations the amount of drug release was compared and it indicates that, the cumulative amount of drug released from F10 was more 99.123±0.146 and it showed sustained action i:e for 48 hrs, For all the remaining formulations it was not attained, this is due to increase in the polymer weight along with increase in the polymer concentration for F10 formulation .

Review of literature gave an idea of using permeation enhancer to improve the drug release from the formulation. The permeation enhancer chooses for the studies were propylene glycol after optimization in formulations F1- F10. The release kinetics was evaluated by making use of zero order, first order, Higuchi's diffusion and Korsemeyer - Peppas equation. Calculated regression co efficient values for different formulations are tabulated in table No- 1.8. These values are compared with each other for model and drug equation. Based on the higher regression values (r^2), the best fit model was zero order for F1 to F10 formulations and the drug release kinetics following Higuchi mechanism. The figure No.1.2– figure No.1.9 shows release kinetic profile of Eletriptan TDDS for zero order, first order, Peppas and Higuchi respectively.

***In-vivo* release studies:** The *in-vitro* release profile data of Eletriptan were given in table No- 1.7, respectively for patches F1 to F10.From these it was seen that F10 is the best formulation which is used for *in vivo* studies in rabbits and the results obtained are shown in the table 1.9. Perusal to figure no-1.3 indicates that 98.967±0.338% of drug was released within 20 hrs from F6. The release kinetics was evaluated by making use of zero order, first order, Higuchi's diffusion and Korsemeyer - Peppas equation. Calculated regression co efficient values are tabulated in table No-1.10. These values are compared with each other for model and drug equation. Based on the higher regression values (r^2), the best fit model was zero order for and the release kinetics following Higuchi mechanism. The figure No-1.10 to figure No-1.13 shows release kinetic profile of Eletriptan TDDS for zero order, first order, Peppas and Higuchi respectively.

Skin irritation studies: Skin irritation studies confirmed that there is no sign of skin reaction after application on rabbit.

CONCLUSION

Eletriptan, an anti migraine agent is selected for the preparation of transdermal delivery system as it complies with physicochemical properties required to permeate through skin. The preformulation studies involving melting point, partition coefficient of the drug were found to be suitable when compared with the standard. The patches were prepared by solvent evaporation method. The patches were subjected for following evaluation parameters such as physical appearance, weight variation, thickness, folding endurance, drug content, percentage moisture absorption, percentage moisture loss, tensile strength, diffusion studies and skin irritation studies. All the parameters shows were within the limits. *In-vitro* drug release the formulations F_1- F_5 , which is containing HPMC- k4 showed better drug release but not lasted upto 48hrs , Among F_6-F_{10} using HPMC-K15 only Formulation F10 which is containing the high polymer concentration showed best drug release which lasted for 48hrs. *In vitro- In vivo* correlation studies are conducted by using the rabbit which established to guarantee the efficiency and bioavailability of the formulation. The graph showed linear curve between *in vitro- in vivo* drug release which indicates good *in vitro-in vivo* correlation.

Table No - 1.1: Results showing Calibration curve of Eletriptan in pH 7.4 phosphate buffer solution

S.No.	Concentration (µg/ml)	Absorbance (225 nm)
1	0	0
2	2	0.124
3	4	0.268
4	6	0.399
5	8	0.558
6	10	0.708

Table No- 1.2: FTIR spectrum of drug, polymer and mixture

S. No.	IR spectrum of	Groups	Peak (cm^{-1})
1	Eletriptan	C-H	2949
		N-H	3371
		C-N	1151
		C=C	1583
		S=O	1342
2	HPMC	C-H	2931
		-OH	3398
		C-O	1062
		CH_2	2839
3	Eletriptan + HPMC	C-H	2943
		N-H	3298
		C-N	1151
		C=C	1583
		S=O	1340

Table No -1 .3: Melting point, solubility, partition coefficient of Eletriptan.

S.No	Parameters	Value of Parameters
1	Melting Point	169 ± 1.15°C
2	Solubility	21.4mg/ml
3	Partition coefficient	10.38

Table No - 1.4: Composition of different formulations containing Eletriptan

Ingredients (mg)	Formulation code									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Eletriptan	40	40	40	40	40	40	40	40	40	40
HPMC-K_4	100	200	300	400	500	-	-	-	-	-
HPMC-K_{15}	-	-	-	-	-	100	200	300	400	500
Propyleneglycol	100	100	100	100	100	100	100	100	100	100
Dibutylpthalate	30	30	30	30	30	30	30	30	30	30
Water	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

HPMC = Hydroxypropyl methylcellulose, q.s = quantity sufficient.

Table No: 1.5-Showing Evaluation Parameters of Appearance, Folding Endurance, Tensile strength, Surface pH, Thickness.

Formulation code/Parameters	Appearance	Folding endurance	Tensile strength	Surface pH	Thickness
F1	Transparent	81±4	2.47±0.04	5.2±0.3	0.197±0.014
F2	Transparent	96±2	2.58±0.02	5.4±0.4	0.198±0.021
F3	Transparent	89±1	2.61±0.02	5.3±0.3	0.202±0.011
F4	Transparent	86±3	2.65±0.08	5.5±0.6	0.224±0.009
F5	Transparent	91±5	2.68±0.06	5.5±0.6	0.285±0.012
F6	Transparent	95±3	2.64±0.08	5.3±0.4	0.228±0.013
F7	Transparent	88±4	2.69±0.07	5.4±0.5	0.232±0.018
F8	Transparent	84±2	2.72±0.06	5.4±0.8	0.241±0.010
F9	Transparent	94±4	2.79±0.09	5.4±0.2	0.268±0.008
F10	Transparent	95±3	2.82±0.07	5.5±0.8	0.295±0.016

n =3

Table No: 1.6 Showing Evaluation Parameters of Moisture content, Moisture uptake studies, Weight variation, *In-Vitro* Drug content, *In-Vivo* Drug content

Moisture content	Moisture uptake studies	Weight variation	*In-Vitro* Drug content	*In-Vivo* Drug content
3.01±0.2	1.29±0.02	17.23±1.02	99.34±0.14	99.27±0.11
3.24±0.2	1.58±0.03	18.22±1.04	99.68±0.18	99.34±0.20
3.18±0.4	1.64±0.02	18.98±1.01	99.73±0.12	99.55±0.67
3.56±0.2	1.68±0.02	19.33±1.02	99.95±0.14	99.61±0.43
3.32±0.3	1.72±0.07	20.46±1.02	99.86±0.15	99.78±0.01
3.41±0.4	1.66±0.08	18.99±1.04	99.65±0.16	99.2±0.04
3.45±0.6	1.71±0.07	19.24±1.02	99.34±0.16	99.08±0.02
3.45±0.3	1.83±0.07	19.97±1.06	98.96±0.12	98.10±0.01
3.51±0.2	1.92±0.04	20.02±1.03	99.45±0.14	99.44±0.21
3.52±0.4	1.96±0.03	20.59±1.05	99.82±0.12	99.79±0.03

n =3

Table No: 1.7 Showing Evaluation Parameters of *In-Vitro* Drug release studies of Eletriptan in Franz diffusion cell using phosphate buffer pH 7.4.

Time	Formulation									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
1 hr	32.76±0.34	24.33±0.09	21.86±0.31	22.50±0.08	15.54±0.34	26.06±0.09	22.10±0.35	17.69±0.34	15.13±0.21	12.52±0.51
2 hr	44.9±0.87	41.23±0.90	28.76±0.12	28.56±0.34	18.50±0.32	32.56±0.24	34.22±0.28	20.57±0.34	22.32±0.11	17.70±0.07
4 hr	57.66±0.60	56.09±0.40	34.35±0.32	32.79±0.31	22.06±0.23	41.17±0.15	48.51±0.98	32.56±0.25	28.65±0.48	23.48±0.17
6 hr	62.10±0.56	62.68±0.60	41.90±0.12	37.57±0.32	28.73±0.24	49.12±0.21	52.51±0.09	38.48±0.79	33.66±0.26	28.55±0.12
8 hr	71.45±0.16	73.66±0.21	48.69±0.41	42.50±0.23	32.74±0.51	56.78±0.37	58.63±0.29	41.68±0.89	37.65±0.37	32.04±0.2
10hr	88.74±0.71	79.09±0.68	52.55±0.30	48.98±0.53	35.17±0.87	61.78±0.49	64.06±0.87	48.46±0.47	42.33±0.47	39.12±0.30
12hr	91.17±0.55	82.97±0.79	64.24±0.78	53.89±0.54	39.06±0.98	75.43±0.29	82.67±0.67	52.35±0.94	49.09±0.54	42.45±0.39
14hr	97.09±0.71	89.75±0.49	71.24±0.80	57.76±0.52	43.57±0.99	82.56±0.95	88.85±0.54	58.26±0.45	51.52±0.87	45.72±0.48
16 hr		91.76±0.12	78.46±0.20	63.56±0.11	49.51±0.35	92.98±0.19	91.48±0.54	61.36±0.34	56.76±0.90	52.57±0.97
18		96.39±0.	82.66±0.	69.76±0.	52.30±0.	98.97±0.	94.91±0.	67.31±0.	59.76±0.	55.57±0.

hr	39	30	12	07	33	09	98	39	01
20 hr		88.78±0.47	72.34±0.31	56.17±0.75	26.50±0.09	98.97±0.68	72.55±0.05	62.57±0.34	58.16±0.06
22 hr		91.58±0.17	78.89±0.81	59.82±0.41		22.10±0.36	78.54±0.34	68.07±0.84	68.75±0.36
24 hr		96.68±0.07	81.67±0.01	63.66±0.27			81.64±0.07	71.57±0.30	70.54±0.59
26 hr		98.59±0.92	86.54±0.13	67.56±0.32			89.12±0.11	76.51±0.46	75.79±0.93
28 hr			88.98±0.76	72.70±0.17			91.06±0.64	78.56±0.99	82.24±0.40
30 hr			92.55±0.98	76.19±0.39			98.99±0.30	82.40±0.04	86.06±0.27
32 hr			96.54±0.12	79.74±0.68				86.58±0.12	89.26±0.47
34 hr			98.87±0.13	82.78±0.40				89.65±0.30	91.26±0.99
36 hr				86.31±0.07				91.43±0.94	94.03±0.98
38 hr				89.53±0.37				94.76±0.34	96.00±0.06
40 hr				93.50±0.45				98.99±0.04	99.12±0.16
42 hr				95.76±0.73					12.62±0.51
44 hr				98.75±0.63					17.75±0.78
46 hr									23.54±0.17
48 hr									28.55±0.10

n=3

Table. N o - 1.8 showing Results of model fitting of Eletriptan TDDS *in-vitro*

Formulation	Zero order	First order	Higuchi matrix	Peppas kinetics
F_1	0.9806±0.013	0.904±0.027	0.9871±0.002	0.9852±0.010
F_2	0.9295±0.004	0.9662±0.007	0.9837±0.005	0.9754±0.007
F_3	0.986±0.007	0.8959±0.034	0.9735±0.001	0.9733±0.002
F_4	0.994±0.005	0.8759±0.013	0.9841±0.002	0.9666±0.001
F_5	0.9973±0.003	0.8549±0.007	0.9867±0.001	0.9698±0.008
F_6	0.9953±0.005	0.7616±0.002	0.9855±0.002	0.9835±0.001
F_7	0.9683±0.004	0.7616±0.004	0.9845±0.001	0.9775±0.002
F_8	0.9938±0.124	0.8093±0.013	0.9870±0.002	0.9862±0.001
F_9	0.990±0.011	0.8693±0.007	0.9773±0.001	0.9699±0.008
F_{10}	0.996±0.005	0.8135±0.002	0.9901±0.002	0.9851±0.001

Table. No- 1.9: Showing Evaluation Parameters of *In-Vivo* Drug release studies of Eletriptan in Rabbit

S.No	Time	% C.R
1	0hr	0
2	1 hr	12.031±0.020
3	2 hr	17.082±0.010
4	4 hr	32.085±0.029
5	6 hr	35.098±0.031
5	10 hr	56.091±0.001

7	23 hr	59.023±0.023
8	24 hr	61.790±0.006
9	28 hr	66.202±0.010
10	32 hr	89.019±0.021
11	36 hr	96.120±0.011
12	48 hr	98.023±0.002

T*-Time, C.R* - Cumulative release, CDR* - Cumulative drug retained

Table . No- 1.10 showing Results of model fitting of Eletriptan TDDS *in-vivo*

S.NO	Formulation	Release kinetics
1	Zero order	0.996±0.005
2	First order	0.8135±0.004
3	Higuchi matrix	0.9901±0.002
4	Peppas kinetics	0.9851±0.001

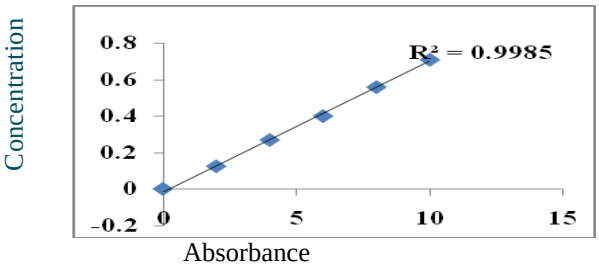


Figure.No-1.1: Graph showing Standard plot of Eletriptan at λmax 225nm

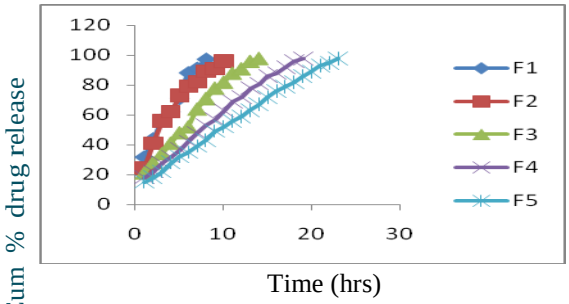


Figure No-1.2: Graph showing Zero order release kinetic profile for F1-F5 formulation

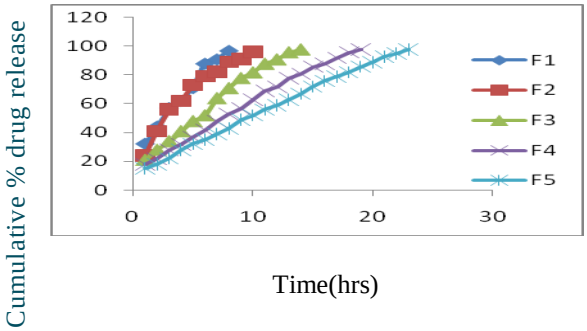


Figure No-1.3: Graph showing Zero order release kinetic profile for F6-F10 formulation

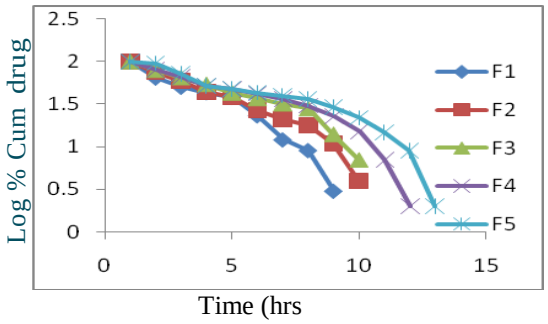


Figure No -1.4: Graph showing First order release kinetic profile of F1-F5 formulation

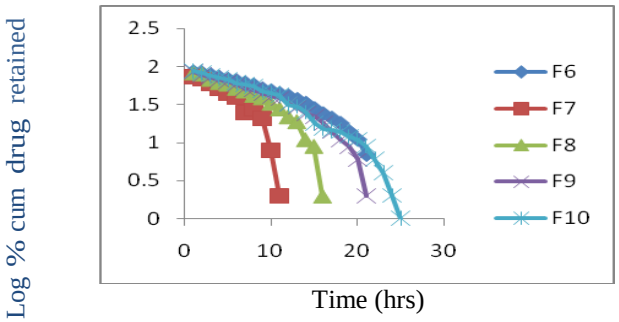


Figure No -1.5: Graph showing First order release kinetic profile of F6-F10 formulation

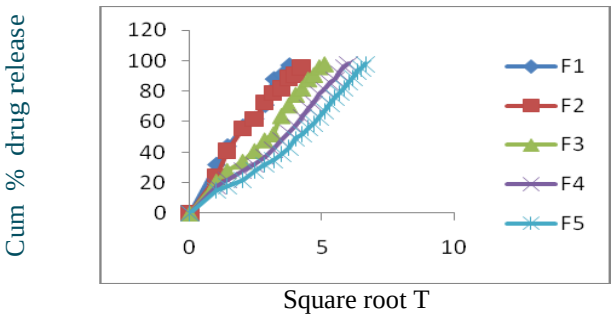


Figure No-1.6: Graph showing Higuchi release kinetic profile of F1-F5 formulation

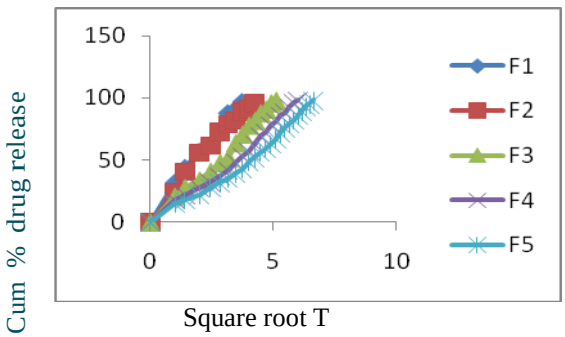


Figure.No-1.7: Graph showing Higuchi release kinetic profile of F6-F10 formulation

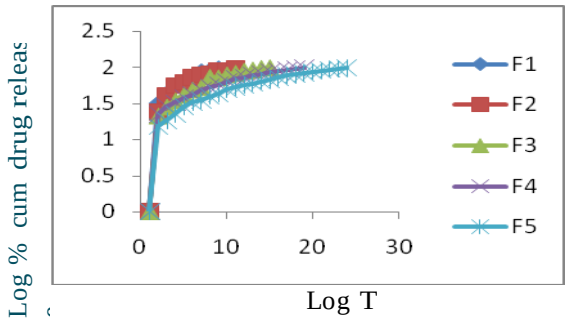


Figure No-1.8: Graph showing Peppas release kinetic profile of F1-F5 formulation

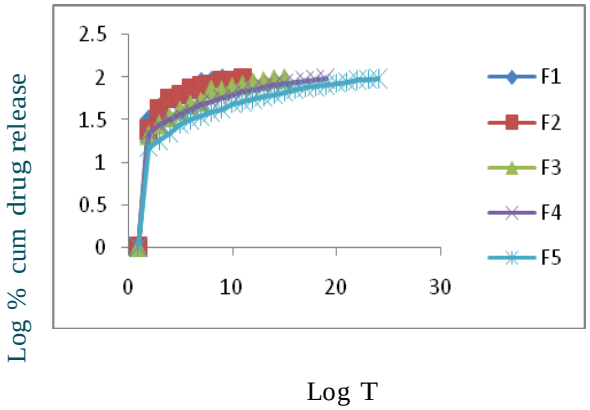


Figure No-1.9: Graph showing Peppas release kinetic profile of F6-F10 formulation

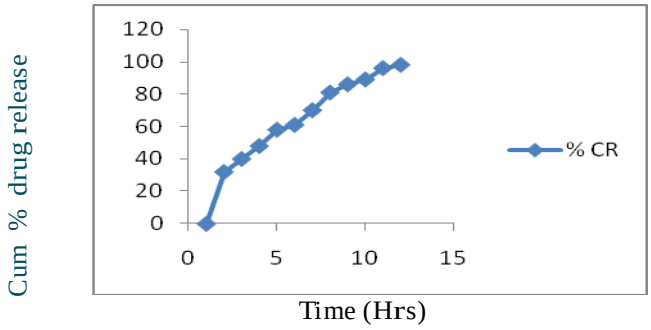


Figure.No-1.10: Graph showing Zero order release kinetic profile of Eletriptan TDDS

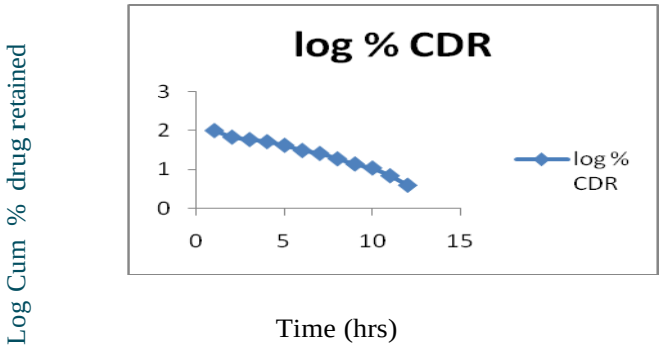


Figure.No-1.11: Graph showing First order release kinetic profile of Eletriptan TDDS

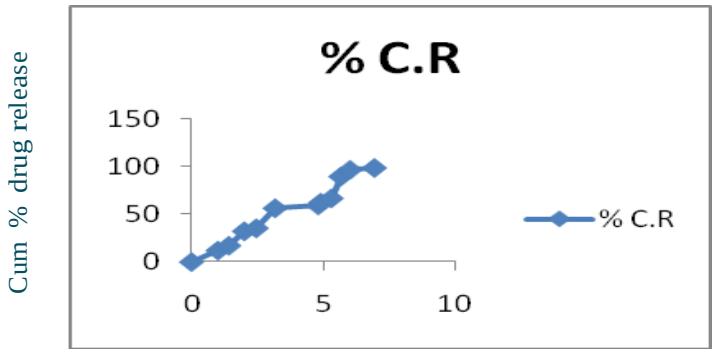


Figure.No-1.12: Graph showing Higuchi release kinetic profile of Eletriptan TDDS

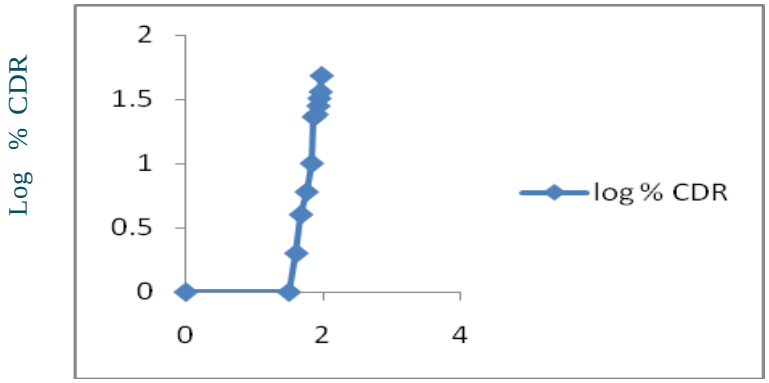


Figure.no-1.13: Graph showing Peppas release kinetic profile of Eletriptan TDDS

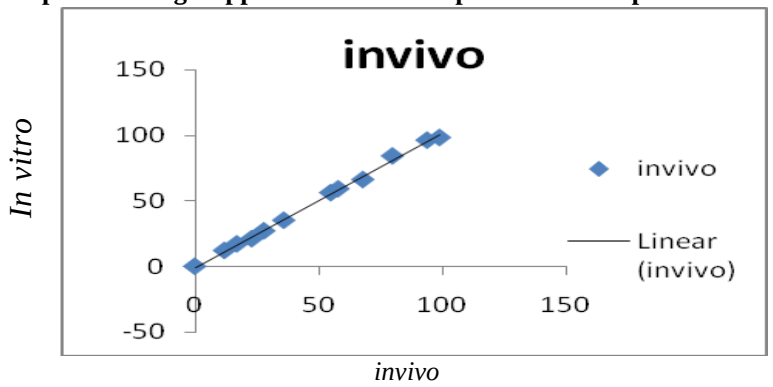


Figure.no-1.14: Graph showing *in vitro-in vivo* correlation of Eletriptan TDDS

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