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Formulation and Evaluation of sustained release Troxipide Matrix Tablets for Twice Daily

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Abstract: The main objective of the present work was to develop sustained release matrix tablets of troxipide using Hydroxy propyl methyl cellulose (HPMC) Varying ratios of drug and polymer like 1:0.5,1:1, 1:1.5, 1:2, 1:2.5 and 1:3 were selected for the study. After fixing the ratio of drug and polymer for control the release of drug up to desired time. After evaluation of physical properties of tablet, the *in vitro* release study was performed in 0.1N HCl pH 1.2 for 2 hrs and in phosphate buffer pH 6.8 up to 12 hrs. The effects of polymer concentration were studied. Dissolution data was analyzed by Korsmeyer-Peppas power law expression and modified power law expression. It was observed that matrix tablets contained drug : polymer ratio 1:2 was successfully sustained the release of drug upto 12 hrs. Among all the formulations, release the drug which follows Zero order kinetics via, swelling, diffusion and erosion and the release profile of formulation F4 was optimized. Stability studies (40±2°C/75±5%RH) for 3 months indicated that Troxipide was stable in the matrix tablets. The FTIR study revealed that there was no chemical interaction between drug and excipients.

Keywords: Troxipide, matrix tablets, anti-ulcer, twice daily, HPMC 15 LV.

Introduction:

Troxipide is a drug used in the treatment of gastro esophageal reflux disease. Troxipide is a novel systemic non-anti secretory gastric cytoprotective agent with anti-ulcer, anti-inflammatory and mucus secreting properties irrespective of pH of stomach or duodenum.

For many decades treatment of an acute disease or a chronic illness has been mostly accomplished by delivery of drug to patient using various conventional dosage forms like tablets, solutions and suspensions, and syrups. Even today these conventional drug delivery systems are the primary pharmaceutical products commonly seen in the prescription and over-the-counter drug market place. This type of drug delivery system is known to provide a prompt release of drug. To achieve therapeutic concentration and also maintain therapeutic concentration desired time done by using polymers. This results in a significant fluctuation in drug levels can be avoided. Novel techniques helpful for capable of controlling the rate of drug delivery, sustaining the duration of therapeutics activity Conventional oral dosage forms often produce fluctuation of drug plasma level that either exceed safe therapeutic level this problem can overcome by matrix tablets.[1] The composition of each tablet is shown in table(1).

Matrix tablet concept has long been utilized to develop sustained- release formulation. The most common method of modify drug release

is to include it in a matrix formulation. Because of their flexibility, hydrophilic polymer matrix systems are widely used in oral controlled drug delivery to obtain a desirable drug release profile4, cost effectiveness, and broad regulatory acceptance. Among the hydrophilic polymers, hydroxypropyl methyl cellulose derivatives are frequently used because of its nontoxic nature, easy compression, swelling properties and accommodation to high levels of drug loading.[2,5] Additionally, HPMC is a pH independent material and hence drug release from hydroxypropyl methyl cellulose matrix formulations is generally independent of processing variables.[2,5]

The Troxipide drug half life was found to be 7.5hrs. The AUC(0-∞) were within the bioequivalence criteria range of 80.00-125.00. [8]

The matrix tablets containing polymer sustained drug release prolong the therapeutic effect. Tablets were prepared by direct compression technology. This technology more advantage in industrial applicability. ([12,13])

MATERIALS AND METHODS

Materials:

Troxipide (shreeji pharma international), HPMC 15LV, magnesium state, talc are analytical grade from my institute. Composition taken for formulation shown in Table 1.

Methods:

The Troxipide matrix tablets were prepared by direct compression method. In this active pharmaceutical ingredients (Troxipide) and inactive ingredients (HPMC, Lactose) are mixed in geometric order. After mixture was pass through sieve #120. Add talc, Mg.sterate sufficient amount compressed in 12 station punching machine with high presser. The obtained tables were evaluated.

Evaluation of tablets:

The prepared tablets were evaluated for weight variation, hardness, thickness, friability, drug content, and In-vitro drug release. [3]

FTIR Studies: IR spectra for Troxipide and formulation (drug+excipients) were recorded in a Fourier transform infrared spectrophotometer (BRUKER). The functional groups are not altered during mixing with excipients. N-H stretching=3500 cm^{-1}, C-H bend (monosubstituted)=993 cm^{-1}, 3900 cm^{-1}, 3744 cm^{-1} are not changed with combination of excipients.[9]

It observed in Figure-1,2 & 3. in this T- Troxipide & TH- Troxipide+HPMC15LV

The FTIR revealed that there is no interaction between drug and polymer.

Calibration curve for Troxipide:

Calibration curve for troxipide prepared in pH1.2 Hcl buffer and in pH6.8 phosphate buffer.

Calibration curve in pH 1.2 Hcl buffer: 10mg of drug (Troxipide) was taken in 100ml volumetric flack dissolved in 25 ml of pH 1.2 solution after soluble completely make up the volume to 100ml (stock solution). From the stock solution 0.5, 1, 1.5, 2, 2.5 and 3 ml taken in 10 ml volumetric flask. Make up the volume to 10 ml with buffer solution. The peak max was observed at 256nm.

Calibration curve in pH 6.8 phosphate buffer: 10mg of drug (Troxipide) was taken in 100ml volumetric flack dissolved in 1ml methanol make up the volume to 100ml with pH 6.8 phosphate solution (stock solution). From the stock solution

0.5, 1, 1.5, 2, 2.5 and 3 ml taken in 10 ml volumetric flask. Make up the volume to 10 ml with buffer solution. The peak maximum in pH 6.8 phosphate buffer was found to be 258.27 nm.

Hardness: Pfizer hardness tester was used for the determination of the hardness. The tablet was placed in contact between the plungers and the handle was pressed, the force of the fracture was recorded. In this work, for each formulation the hardness of 6 tablets was evaluated. The results were observed in table-2.

Weight variation: In weight variation test twenty tablets were selected at a random and average weight was calculated. Then individual tablets were weighed and the weight was compared with an average weight. The results were observed in table-2.

Thickness: The crown-to-crown thicknesses of ten tablets from each batch were determined using vernier calipers. The results were observed in table-2.

Friability: The Friability of the tablets was determined using Roche friabilator (Electrolab). This device subjects the tablets to the combined effect of abrasions and shock in a plastic chamber revolving at 25 rpm and dropping the tablets at a height of 6 inches in each revolution. Weighed sample of tablets was placed in the friabilator and were subjected to 100 revolutions. Tablets were de-dusted and reweighed.

The friability (F) is given by the formula: $F = (1- W0 / W) \times 100$

Where, W0 is the weight of the tablets before the test and W is the weight of the tablet after the test. The results were observed in table-2.

Drug content: For determination of drug content at least two tablets from each formulation were weighed individually, pulverized, and diluted to 250ml with sufficient amount of phosphate buffer pH 6.8. After that an aliquot of the filtrate was diluted and analyzed spectrophotometrically at 256nm. The results were observed in table-2.

In vitro drug release studies: [10]

In vitro drug release studies for the prepared matrix tablets were conducted for a period of 12 hrs using a 8 station USP -2 (LABINDIA DS8000.) apparatus at 37±0.5oC and at 100 rpm speed, the in vitro release study was performed in 0.1 N HCL pH 1.2 for 2 hrs and in phosphate buffer pH 6.8 up to 12 hrs. At every interval 5 ml of sample was withdrawn from the dissolution medium and replaced with fresh medium to maintain the volume constant. After filtration and appropriate dilution, the sample solutions were analyzed at 256 nm for Troxipide by a UV-Visible spectrophotometer. The amount of drug present in the samples was calculated. The results were observed in table-3, and graph-1. Kinetics of drug release from formulation was described in the table-4.

Results and discussions:

In the troxipide matrix tablets formula F4 release drug 91.88% for 12hrs, so it was optimized all the 6 formulations. F1 release completely with in 5hrs. F2 formulation drug release was found to be 90.89% within 6hrs. F3 formulation drug release was found to be 91.58% at 7 hrs. F5 and F6 formulation drug release was found to be 83.03 & 61.22 % respectively.

Table 1: Composition of sustained release Troxipide matrix tablets.

Ingredients	F1(1:0.5)	F2(1:1)	F3(1:1.5)	F4(1:2)	F5(1:2.5)	F6(1:3)
Troxipide(mg)	150	150	150	150	150	150
HPMC(mg)	75	150	225	300	375	450
Lactose (mg)	375	300	225	150	75	-
Talc (mg)	12	12	12	12	12	12
Mg.sterate (mg)	6	6	6	6	6	6

Table 2: Evaluation parameters

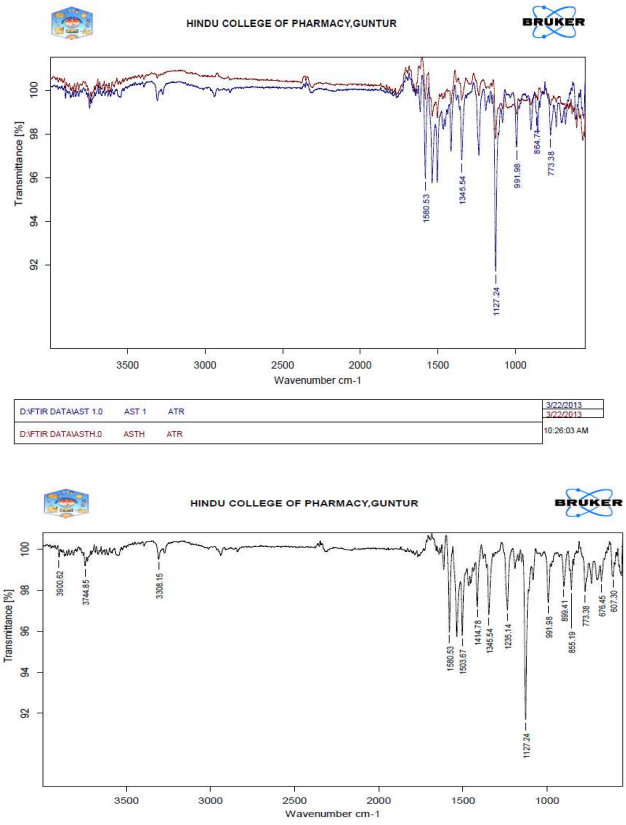
Formulation	Hardness (kg/cm^3)	Weight variation	Thickness (mm)	Friability	Drug content
F1	7.2±0.5	pass	3.52±0.2	0.5±0.05	99.25±0.75
F2	6.8±0.5	Pass	3.52±0.2	0.7±0.05	98.95±0.75
F3	7.1±0.5	Pass	3.52±0.2	0.9±0.05	99.21±0.75
F4	6.9±0.5	Pass	3.52±0.2	0.5±0.05	98.89±0.75
F5	7.4±0.5	Pass	3.52±0.2	0.6±0.05	99.56±0.75
F6	7.2±0.5	Pass	3.52±0.2	0.8±0.05	100.21±0.75

Table 3: Cummulative % drug release

time	F1	F2	F3	F4	F5	F6
0	1.24	1.59	0.967	0.924	1.311	1.22
1	20.3	27.29	17.45	11.25	8.8	8.41
2	29.97	34.95	27.36	17.69	13.54	12.44
3	32.58	38.35	31.2	20.45	15.68	14.92
4	89.14	57.12	61.19	28.79	22.7	21.39
5	96.11	74.23	76.19	56.36	45.15	27.73
6		90.89	87.37	60.96	53.69	46.49
7			91.58	67.28	59.22	49.39
8				71.36	62.9	53.46
9				76.75	67.11	56.36
10				79.9	69.35	58.2
11				85.3	75.66	59.78
12				91.85	83.03	61.22

Table 4: Release kinetics of Troxipide matrix tablets (F1-F6)

Model	Parameter	F1	F2	F3	F4	F5	F6
Zero order	R^2	0.857	0.952	0.956	0.941	0.948	0.925
First order	R^2	0.794	0.842	0.927	0.954	0.965	0.955
Higuchi	R^2	0.754	0.899	0.884	0.921	0.905	0.903
Korsmeyer peppas	R^2	0.827	0.892	0.944	0.952	0.948	0.952



Troxipide IR study

IR spectrum of formulation

Figure-1 T-Troxipide, TH- Troxipide+ HPMC 15 LV

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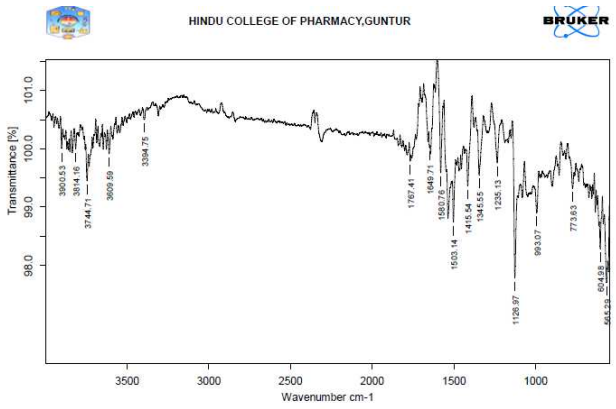
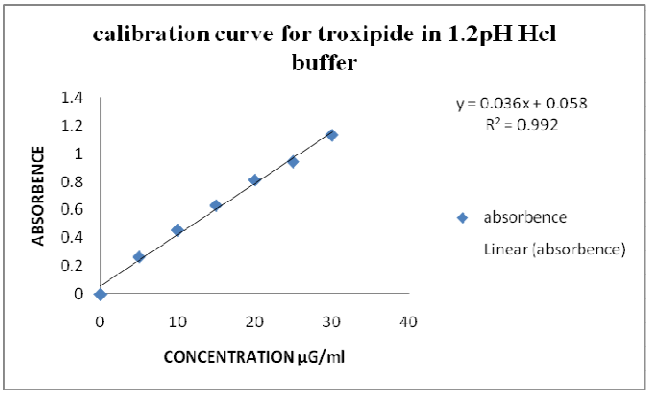
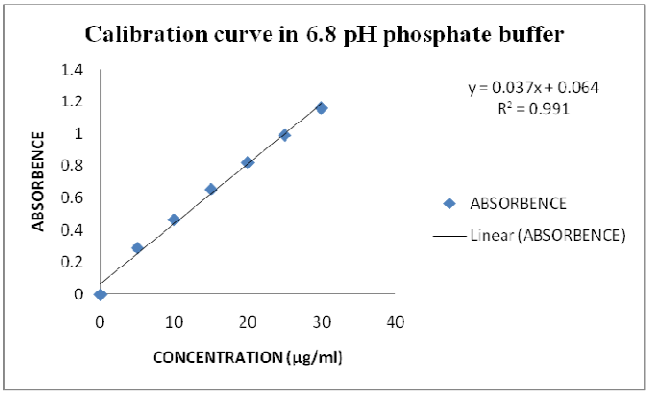


Troxipide +HPMC

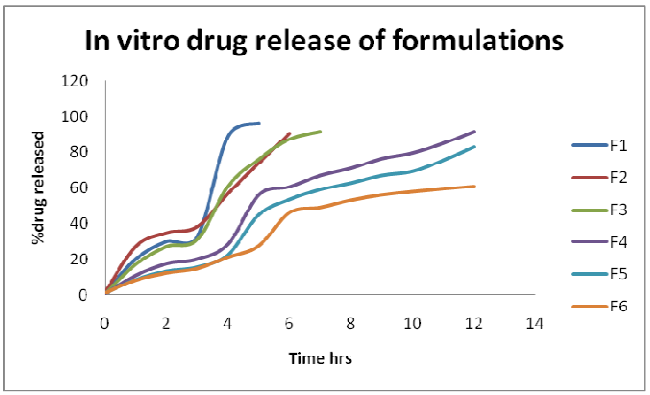
Graph-1



Graph-2

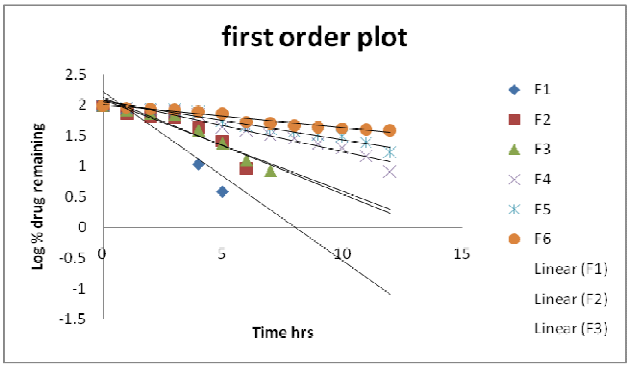


Graph -3

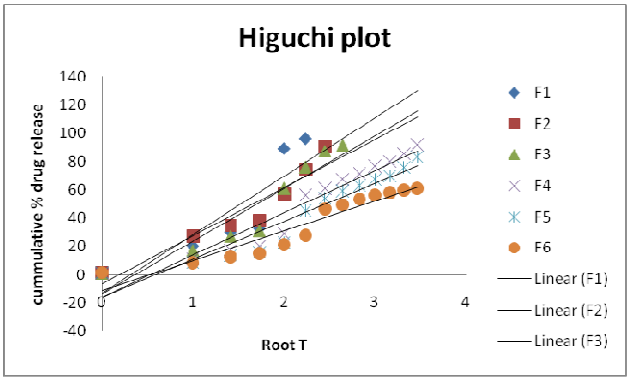


Graph -4

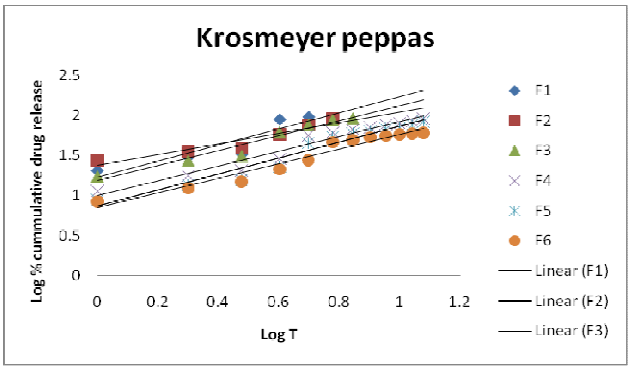
Graph-5



Graph-6



Graph- 7



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Conclusion:

In the formulation of troxipide matrix tablets revealed that, due to increase polymer concentration drug release was found to be prolong. The anti ulcer activity was prolonged by this formulation. With the other natural and synthetic polymers can be used for prolong the therapeutic effect of Troxipide. The polymers play an important role in the release of drug from formulation.

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