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FORMULATION AND EVALUATION OF SUCRALFATE AND METOPROLOL SUCCINATE BI-LAYER FLOATING TABLET AS GASTRO RETENTIVE DRUG DELIVERY SYSTEM

Sreedhar Ranjan Das[1*], Dr. Bibhuti Bhusan Panigrahi[2] and Dr. Manoj Kumar Pani[2]

PG Department of Pharmaceutics, Indira Gandhi Institute of Pharmaceutical Sciences, Bhubaneswar.

***Corresponding Author: Sreedhar Ranjan Das**

PG Department of Pharmaceutics, Indira Gandhi Institute of Pharmaceutical Sciences, Bhubaneswar.

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ABSTRACT

The present research deals with formulation and evaluation of Bi-Layer Floating Tablet of Ulcer protective Sucralfate as Immediate Release Layer and Antihypertensive Metoprolol Succinate as Floating Sustained Release layer. This formulation generate maximum bioavailability and prolonged gastro retention and satisfy GRDDS in patients having Stomach Ulcer with Hypertension in pregnancy and lactation. Both the drugs are administrated in empty stomach and shows minor drug interaction. The present research based upon Spectral analysis, Identification test and Preformulation study of pure drug. Then Formulation, In vitro evaluation, Accelerated stability study of 15 formulations of Sucralfate and 10 formulations of Metoprolol Succinate are done and the best formulations are selected as SF13, MS2. Then Bi Layered floating tablet is compressed and In vitro and In vivo evaluation is done and accelerated stability is done and it is confirmed that the formulation produce better GRDDS.

KEYWORDS: Sucralfate, Metoprolol Succinate, GRDDS, Stomach ulcer, Hypertension, Pregnancy & lactation.

INTRODUCTION

Bi-layer Floating Tablet comes under floating system which was described by Davis-1986.[1] It contain Immediate release layer which deliver initial dose by increasing lag time.[3] Another layer is Sustained release layer which remain in gastric region[2] for several hours and prolong the gastric resistance time and produce buoyancy[3] and improve bioavailability at high PH environment. Hypertension [4] is most common medical problem during pregnancy by which up to 10% of pregnancies are affected. Stomach ulcer[5] is a great problem in pregnancy which occurs heart burn, nausea, vomiting, abdominal pain, black stool etc.

Sucralfate is basic aluminium salt[6] of sulphated sucrose which polymerise at PH <4 by cross linking of molecules assuming gel like consistency and provide surface protein at ulcer base and act as physical barrier preventing acid, pepsin and bile coming contact with ulcer base. It can be administered in empty stomach (1 gm before 1 hour of mill). It has no acid neutralizing action but delay gastric emptying and remain in stomach for 6 hours. It can also be administered in case of pregnancy and lactation. So it the drug used for treatment of stomach ulcer in case of pregnancy.

Metoprolol Succinate is a drug[7] from the group of selective β-1 blockers. It is the first choice drug in the treatment of mild to moderate Hypertension and Angina pectoris. It is also used for heart muscle damage in patient after myocardial infraction. It is more efficient for treatment of blood pressure[4] in pregnancy and lactation because it having low risk of adverse effect on uterus. The starting dose[8] is 100mg once a day and maintenance dose is 200 mg daily[9] in empty stomach with 200 ml of water.

Both of drugs; Sucralfate and Metoprolol Succinate[8] can be implemented in pregnancy as well as in case of lactated mother also. Both the drugs are administered in empty stomach and produce very minor drug interaction.[9] The combined form as Bi-layer Floating Tablet can be used in treatment of stomach ulcer with hypertension[10,11] in pregnancy and lection.

The objectives of this present research to formulate and evaluate the Bilayer Floating Tablet with fulfilment of post comprisal parameters; Tablet Consistency, Floating Lag Time,[12] Tablet Floating Time, Swelling index, Drug release etc. and to form a better formulation of GRDDS.

MATERIALS AND METHODS

According to different properties and uses of various exepients are taken in different ratios to formulate and optimize Bi-layered Floating Tablet of Sucralfate and Metoprolol Succinate.[T-1,T-2].

1-Spectral analysis of pure drug[12]

1.1-Spectral analysis of pure drug of Sucralfate through UV visible spectrophotometer is done and the wavelength at which maximum absorbance is produced is determined. The standard stock solution of pure drug of Sucralfate is done by 25mg of pure drug was accurately weighed and transferred to well cleaned and dried 100ml volumetric flask. To this 25ml of methanol was added and agitated well until the drug dissolves completely. The remaining volume was made up to 100ml with different buffers separately in each case (0.1N HCL, and 6.8pH phosphate buffer respectively). Spectrophotometric scan was performed for the prepared diluted sample to find out λ_{max} in the wavelength region 200-800 nm. The λ_{max} was found to be 281 nm against blank solution.[Fig1] Standard curve of Sucralfate in PH 6.8 and in 0.1N HCL at 281nm is done.[T3T4Fig2,Fig3]

1.2-Spectral analysis of pure drug of Metoprolol Succinate through UV visible spectrophotometer is done and the wavelength at which maximum absorbance is produced is determined. The standard stock solution of Metoprolol Succinate is done by100mg of pure drug of Metoprolol was accurately weighed and transferred to well cleaned and dried 100ml volumetric flask. To this 25ml of 0.1N HCL was added and shaked well until the drug dissolves completely. Then the remaining volume was made up to 100ml with 0.1N HCL. Spectrophotometric scan was performed for the prepared diluted sample to find out λmax in the wavelength region 200-800 nm. The λmax was found to be 233 nm against blank solution. [Fig4]. Standard curve of of Metoprolol Succinate in 6.8 PH phosphate buffer at 233 nm is done.[T5, Fig 5].

2-Preformulation study[13]

The preformulation studies like flow properties, solubility and drug-excipient compatibility studies were determined.

Flow properties of Sucralfate, Metoprolol Succinate pure drug[T6,T7]

The following flow properties of the pure drug and granules were evaluated.

Bulk density and Tapped density (g/ml)

The previously weighed pure drug or granules (W) were placed separately into a graduated measuring cylinder and the initial (bulk) volume (V_B) was noted. It was placed in the tapped density tester USP and subjected to constant tapping at a rate of 200drops/min until the difference between the initial and final volumes should be less than 2%. It was recorded as the final (tapped) volume (V_T) and various flow properties were calculated with the following formulae.

Bulk density, $\rho B = \frac{W}{VB}$, Tapped density, $\rho T = \frac{W}{VT}$

Compressibility Index

It was calculated by using the following formula

Carr's Index or Compressibility Index (CI) = $1-\frac{\rho B}{\rho T} * 100$

The CI value below 15% indicates good flow of the powder and above 30% indicates poor flow property of the powder.

Hausner's Ratio: It is calculated by the following formula;

Hausner's Ratio= $\frac{\rho T}{\rho B}$

The Hausner's ratio below 1.25 indicates good flow property and above 1.25 indicates poor flow property of the powder.

Angle of Repose (Ɵ): It was determined by using a funnel whose tip was fixed at a constant height (H) of 2.5cm from horizontal surface. The granules and the powder were passed separately through the funnel until the tip of the conical pile touches the tip of the funnel. The radius of the base of the conical pile is measured as R (cm). It is determined with the formula;

Angle of repose (θ) = Tan^{-1} (height /radius).

3- Identification of Sucralfate and Metoprolol Succinate by FT-IR[14]

Fourier-transform infrared (FT-IR) spectra wereobtained using FTIR (Bruker, Germany) The pure Sucralfate and Metoprolol were mixed separately with potassium bromide, an infrared transparentmatrix, at 1:5 (Sample: KBr) ratio, respectively. The KBr discs were prepared by compressingthe powders at a pressure of 5 tons for 5 min in a hydraulic press. [Fig 6, Fig 7].

4- Preparation of granules

4.1. Preparation of Sucralfate granules

The15 formulations of Sucralfate IR tablets were prepared by wet granulation method**.** The composition of the tablet is mentioned in[T8,T9]. The required ingredients were weighed accurately and passed through 40 mesh. The sieved materials were then mixed well in a poly bag for about 30 minutes. The surfactants, SLS and polysorbate80 were dissolved in cold and hot water respectively to use as granulating fluid. To moisten the blend, either water or surfactant solution was used as granulating fluid. The wet mass was granulated in RMG granulator. The granules were then dried in a Retsch rapid dryer at 60^0C for about 60 minutes until the % LOD becomes less than 3%. The dried granules were then passed through 40 mesh and then lubricated by mixing with the lubricant (which was previously passed through 60 mesh) in a polybag for about 15 minutes. The flow properties of the lubricated granules were determined.

4.2. Preparation of Metoprolol Succinate granules

The Metoprolol Succinate floating SR tablets were prepared by wet granulation method. The composition of the tablets is given in [T10]. The drug and polymer which were previously passed through 40 mesh were mixed thoroughly in a polybag for 20 minutes. The blend was moistened with granulating fluid *i.e.*, water and IPA (1:9 parts). The wet mass was passed through 24 mesh and then dried in a tray dryer at 50^0C for about 50 minutes until the % LOD becomes less than 2%. The dried granules were passed through 30 mesh and mixed with sodium bicarbonate in a polybag for 10 minutes. To this talc (previously passed through 60mesh) was added and mixed well for 10 minutes. The flow properties of the lubricated granules were evaluated.

4.3. Flow Properties of Lubricated granules

The lubricated granules obtained from wet granulation of Sucralfate and Metoprolol Succinate with different excipients are evaluated for flow properties like bulk density, tapped density, compressibility index, Hausner's ratio and angle of repose. [T-11,T-12]

5- Acclerater stability study of Lubricated Granules[15]

Acclerated stability study is done of lubricated granules 10 gm of each formulations of Sucarlfate and Metoprolol Succinate at at 45^0C and 75% RH for a period of 3 months. The granules were packed in 85mm HDPE bottles with an oxygen adsorbent, and a desiccant containing silica gel with cotton as filler. The granules were withdrawn after the regular interval of stability period, and evaluated for physical properties.[T13,T14]

5.1 – Compairision study is done between initial parameters of flow properties of granules and granules after 90 days of stability study.of Sucralfate and Metoprolol Succinate.[T^{15},T^{16}] To develop the flow properties of SF3,SF5,SF6,SF9,SF10,SF13,MSF2, MSF8,MSF9 5 gram of talc is added in each formulation.

6- Preparation of Tablet[16]

6.1-Preparation of Sucralfate (IR) layer in BIlayer Floating Tablet

The lubricated granules were then compressed by using 16 station tablet compression machine (CADMACH) with 7mm plane round shaped punches. 15 formulations of Sucarlfate tablet are made of different compositions.[T8,T9]

6.2-Preparation of Metoprolol Succinate (SR) tablet

The lubricated granules were compressed by 16 station tablet compression machine (CADMACH) with 13.1mm round concave punches. The 10 formulations of different compositions are made.[T10]

7-Evaluation of tablets[17,18]

The Post comprisal parameters[T-17,T-18] like hardness, thickness,% friability, disintegration time were evaluated for all the prepared tablets. The drug content was determined for all the batches. Dissolution studies were conducted for all formulations.

7.1-Weight variation

Twenty tablets were collected randomly and the average weight and individual weight was calculated. The % weight variation was calculated with the following formula.

%Weight variation= Average weight-individual weight/individual weight x100

7.2-Thickness

The thickness of the ten tablets was measured in mm by using Vernier calipers.

7.3-Hardness

The hardness of the ten tablets was measured by using Varian V K200 Tablet Hardness Testerand is given in the units of KP.

7.4-% Friability

Ten tablets were carefully dedusted prior to testing and weighed accurately (Wo). The tablets were placed in the drum of Roche Friabilator (USP). The drum was rotated for 100 times at a speed of 25rpm. The tablets were collected, re-dedusted and accurately weighed (W1). It is calculated form the following formula;

$$\% \text{ Friability} = 1 - \frac{W1}{W0} * 100$$

7.5-Disintegration Test

The disintegration study was performed for sucralfate tablets by using disintegration apparatus Thermonik DT Tester (USP). For this water was used as the disintegration medium. 6 tablets were placed in 6 tubes of the disintegration apparatus. The time (min) taken for the tablets to disintegrate was noted.

7.6-Floating lag time (FLT)

The MS tablets were placed in a beaker containing 250ml of 0.1N HCl and the time (sec) required to float the tablet was observed and recorded as FLT.[T18].

7.7-Total floating time (TFT)

The time (hr) up to which the MS tablet remains buoyant was noted and recorded as TFT. [T18].

7.8 -Determination of swelling index of Metoprolol Succinate tablets[T-19]

The previously weighed (W1) tablet was placed in USP apparatus type-I which was immersed in a bowel containing 900ml of 0.1N HCl and maintained at 37 ± 0.2^0C. The tablets were removed from the basket at regular intervals of time (up to 8hrs with 1 hr interval) and placed on a blotting paper to remove the excess medium (Fig 6.7). The tablet was reweighed (W2). The studies were repeated for all formulations in triplicate. The swelling index was calculated as follows: [T17].

Swelling Index = W2-W1/W1 x 100

7.9-Determination of drug content of Sucralfate tablets [T17]

Ten SF tablets were weighed accurately and then crushed well in a clean motor and pestle. The powder equivalent to 25mg of the drug was weighed (Ws) and then transferred to a 100ml volumetric flask. 50ml methanol was added and sonicated for 5 minutes at 27^0C. Then the volume was made up to 100ml using methanol (V4). From this 4ml (V5) was transferred to a 100ml volumetric flask and the volume was made up to 100ml (V6) with 0.1N HCl (pH 1.2). The flask was agitated for 5 minutes and then the sample was analyzed for drug content at 281nm using UV Spectrophotometer. The drug content was calculated using the following formula.

$$\% \text{ Drug Content} = \frac{AS}{AS} * \frac{W}{V1} * \frac{V2}{V3} * \frac{V4}{WS} * \frac{V6}{V5} * \frac{AW}{L} * P$$

Where,
AS= Test absorbance
AS= Standard Absorbance
W= Weight of standard drug (25mg)
V1= Volume of solvent added to standard stock solution (100ml)
V2, V3= Dilution of the standard stock solution (4ml of stock solution diluted to 100ml with solvent)
AW= Average weight of the tablet (mg)
L= Label claim of the drug (10mg)
P = Potency of sucralfate (91.4%).

7.10-Determination of drug content of Metoprolol Succinate tablets[T18]

Ten MS tablets were weighed and crushed in a motor with pestle. The crushed powder equivalent to 100mg of MS (WS) was weighed accurately and transferred to a clean, dried 100ml volumetric flask. 50 ml of 0.1N HCl was added and agitated vigorously for 10 minutes and sonicated for 4 hours. The final volume was made up to 100ml (V4) using 0.1N HCl and agitated for 5 minutes. A portion of it was centrifuged at 3000rpm for 10 minutes. The centrifuged sample was filtered through 0.45µm whatmann filter paper. 2 ml (V5) of the filtered sample was pipetted out and transferred to a 100ml volumetric flask and the volume was made up to 100ml (V6) with 0.1N HCl and the flask was shaked for 5 minutes. The sample was then analyzed for the drug content at 233nm using UV Spectrophotometer. The drug content was calculated using the following formula.

$$\% \text{ Drug Content} = \frac{AS}{AS} * \frac{W}{V1} * \frac{V2}{V3} * \frac{V4}{WS} * \frac{V6}{V5} * \frac{AW}{L} * P$$

AS= Test absorbance
AS= Standard Absorbance
W= Weight of standard drug (100mg)
V1= Volume of solvent added to standard stock solution (100ml)
V2, V3= Dilution of the standard stock solution (2ml of stock solution diluted to 100ml with solvent)
Aw= Average weight of the tablet (mg)
L= Label claim of the drug (375mg)
P = Potency of metoprolol succinate (99.83%).

7.13- Release kinetic profile of Metoprolol Succinate Mechanism of drug release from MS tablets

Different mathematical models were applied for describing the kinetics of the drug release process from the tablets. The rate of drug release from tablets was determined by finding the best fit of the dissolution data to distinct models: zero order (eq. 1), first order (eq. 2), and mechanism of drug release from Higuchi (eq. 3) and Peppas (eq. 4) models.

$Qt = k0\ t$---------(eq. 1) $Qt = Q\infty\ (1\text{-}e\text{–}k1t)$----------(eq. 2)
$Qt = kH\ t1/2$-------(eq. 3) $Qt= kt^n$ or $logQ=logk+nlogt$---(eq. 4)

Where, $Q\infty$ being the total amount of drug in the matrix, k0 the zero order kinetic constant, k1 the first order kinetic constant and kH representing the Higuchi rate constant. The best fit model was found by using correlation coefficient values (R), using MS EXCEL.

The data obtained from in vitrodissolution studies werefitted to zero-order, first-order, and Higuchi and Korsemeyer–Peppas equations. The dissolution data obtained wereplotted as Time versus cumulative percent drug released aszero order, Time versus cumulative percent drug remaining as First order release kinetics, Square root oftime versus cumulative percent drug released as Higuchiequation and Log time versus log cumulative percent drug released as per Korsemeyer-Peppas equation. were studied.

The comparative cumulative zero order, first order, higuchi model and pappas model plots of F1 to F10 formulations respectively. The release data from [MSF2 and MSF9]fitted in to Higuchi model and the others[MSF3, MSF4, MSF5, MSF6, MSF7,MSF8 and MSF10] followed Peppas mechanism[Fig-8,Fig-9,Fig10,Fig11].

7.14- Acclerated stability study is done of 10 Tablets of each formulations of Sucarlfate and Metoprolol Succinate at at 45^0C and 75% RH for a period of 90 Days..The tablets were packed in 85mm HDPE bottles with an oxygen adsorbent, and a desiccant containing silica gel with cotton as filler. The granules were withdrawn after the regular interval of stability period, and evaluated for physical properties.[T20,T21]

8-Selection of best formulation of Sucralfate and Metoprolol Succinate

According to Accelerated stability study of lubricated granules and Post compressional parameters and Accelerated stability study of compressed tablets one formulation of Sucralfate and one formulation of Metoprolol succinate is selected.

8.1 Acclerated stability study lubricated granules

Acclerated stability study lubricated granules is done of lubricated granules of selected formulations of Sucarlfate and Metoprolol Succinate at at 45^0C and 75% RH for a period of 3 months. The tablets were packed in 85mm HDPE bottles with an oxygen adsorbent, and a desiccant containing silica gel with cotton as filler. The granules were withdrawn after the regular interval of stability period, and evaluated for physical properties [T22].

9-Preparation of Bi-layered tablets of SFMS

Sucralfate layer and Metoprolol Succinate layer, Bilayered Floating tablets were prepared.The Bi-Layered tablets of Sucralfate and Metoprolol Succinate (SFMS) were compressed using 13.1mm round concave punches using a Bi-Layered Tablet Compression Machine. The granules of Metoprolol Succinate were placed first and pre-compressed with slight hardness of about 4-5KP. Then the granules of Sucralfate were placed and compressed with a final hardness of about 12-14 KP. The compression of Bi-Layered Tablet is based upon Composition of optimized Sucralfate layer and composition of optimized Metoprolol Succinate layer.

9.1- The post compressional parameters of SFMS tablets[T23]

The post compressial parameters; Average weight, Thickness, Hardness,% friability, FLT, TFT, DT of Sucralfate Layer is determined.[T23]

9.2- Acclerated stability study of SFMS bi layered tablets

10 Tablets of SFMS Bi-layered tablets were subjected to accelerated stability studies at 45^0C and 75% RH for a period of 90 Days. The tablets of SFMS were packed in 85mm HDPE bottles with an oxygen adsorbent, a molecular sieve and a desiccant containing silica gel with cotton as filler. The tablets were withdrawn after the stability period, and evaluated for physical properties like weight variation, thickness, hardness, % friability, disintegration time of SF layer, FLT and TFT of MS layer and in vitro drug release studies.[T24]

10-In –Vivo Evaluation Test

In-vivo X-Rays Studies (Radiographic imaging technique)

10.1-Animal care and handling

The experiment was carried out on Healthy white rabbits of 12 months, weighing between 1.5-2.0kg. The animals were acclimatized to the standard laboratory conditions in cross ventilated animal house at temperature 25±2°C relative humidity 44-56% and light and dark cycles of 12:12 hours, fed with standard pellet diet and water ad libitum during experiment. The animal protocol was approved by the institutional ethics committee and as per Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) guidelines.

10.2-Procedure[19,20,21]

The rabbit was fasted 24 h prior (overnight fasted) to experiment and allowed free accesses to water only. The floating property of the selected floating tablet was studied by radiographic imaging technique under the guidance of a qualified radiologist.To make the tablet X-Ray opaque,barium sulphate ($BaSO_4$) was incorporated in tablets. Barium sulphate has a high density (4.4777 g/cm^3) and poor floating properties. The tablets prepared for radiographic imaging contained (rabbit dose, 80mg/kg) where a part of the drug was replaced with $BaSO_4$ for in vivo studies. A wooden block with central opening was placed between upper and lower teeth of rabbit and tablet was administered orally using oral gavages by the help of a hollow tube made up of polyethylene. The tube was inserted into the mouth of rabbit and blown using rubber bulb. About 5-10 ml of water was further administered (flushed) to ensure the complete delivery of the dosage form.

X-Ray photographs were also taken for the rabbits before giving the dosage form (pre-treatment) to ensure that no material containing Barium sulphate was present in the stomach and these photographs served as control. After the ingestion of the tablet, the rabbits were exposed to X-Ray photography in the stomach region. X-rays photographs were taken under the guidance of a qualified radiologist at different time intervals for 0, 1, 2, 4, 6 hours.

X-ray imaging was done at 40mA, 45KV, and 5mAs (Genius-60 Mobile portable unit, Wipro GE Medical Systems Ltd., Pune, India). The distance between the source of X- ray and rabbit abdomen was kept constant (80 cm) for all images.

RESULT AND DISCUSSION

1. Spectral analysis of pure drug

By the spectral analysis through UV-visible spectrophotometer, the wavelength of Sucralfate shows maximum absorbance as 281 nm and Metoprolol Succinate shows maximum absorbance as233nm**.**[T3,T4,T5,Fig1,Fig2,Fig3,Fig-4,Fig5]

2. Preformulation studies

The preformulation studies of Sucralfate and Metoprolol Succinate pure drug are studied individually which shows better flow properties.[T6,T7].

3. Identification of Sucralfate and Metoprolol Succinate by FT-IR

Fourier-transform infrared (FT-IR) spectral analysis of pure Sucralfate and Metoprolol Succinate individual mixture produce satisfactory result.[F6,F7]

4-Flow Proreties of lubricated Granules

The lubricated granules obtained from wet granulation of Sucralfate and Metoprolol Succinate with different excipients are evaluated which produce better flow properties.[T11,T12].

5- Accelerated stability study of Lubricated Granules
After 90 days some negligible changes occurred in physical parameters; Slide yellowish, Rare black spots, Started melting, Odour change, Agglomeration, Started caking, Stick at the wall etc. But these are very negligible. So we except it will not produce more impact on optimization[T13,T14] and it can be recovered after optimization.

6-After that compairsion study is done between initial parameters of flow properties of granules and flow properties of granules after 90 days of stability study. of Sucralfate and Metoprolol Succinate [T15,T16]. we found that there is very slide change in parameters of flow properties of granules which has no more impact on optimization.

7-Evaluation of Tablets
The Post compressional parameters of Sucralfate Tablets[T17]
It shows SF13 produce better disintegration time 0.51±0.079 min and drug content is 99.15%. and fulfil the other parameters.

The Post compressional parameters of Metoprolol Succinate Tablets
Buoyancy study of Metoprolol Succinate
In vitro Buoyancy study of MSF2 shows Floating Lag Time 16 Sec and Total FloatingTime >20 hours.[T18].

Swelling index of Metoprolol Succinate
Swelling index values observed from MSF2 shows 255.% at 8 hours.[T19].

Drug content of Sucralfate and Metoprolol Succinate Tablets
Drug content of each formulations of Sucralfate and Metoprolol Succinate Tablets shows more than 98% of drug release.[T17,T18].

Acclerated stability study of Sucralfate and Metoprolol Succinate Tablets
Accelerated stability shows there is some negligible change in colour or some black spots were observed in some formulations.So we except it will not produce more impact on optimization of further formulations and it may be recoverable on further optimization.[T20,T21].

Release kinetic profile of Metoprolol Succinate
The best fit with the highest determination R^2 coefficients was shownby both zero order models and Higuchimodel followed by Korsemeyerpeppaswhich indicate the drug release via diffusion nmechanism. Zero-order rate equations, which describe the system where release rate is independent of the concentration of the dissolved species. The Korsemeyerpeppas equation is used to analyze the release of pharmaceutical polymeric dosage forms, From the result it was confirmed that all the formulations are following higuchi model which indicate the drug release via diffusion mechanism. The slope value from korsemeyer plots confirmed that the formulations are following Fickian diffusion. [Fig8,Fig9,Fig10,Fig11].

8-Selection of best formulation of Sucralfate and Metoprolol Succinate
According to Accelerated stability study of lubricated granules and post compressional parameters and Accelerated stability study of compressed tablets SF13 and MSF2 is selected.[T-22,T-23].

9-The accelerated stability study of granules of optimized formulations
The accelerated stability study of granules of optimized formulation of Sucralfate and Metoprolol Succinate provide there is no change in physical parameters after 90 days.[T24].

10-Post compressional parameters of SFMS Bilayered Floating Tablet
After optimization of Sucralfate and Metoprolol Succinate formulations The Bilayered Floating Tablet is prepared and post compressional parameters are studied and found that the Disintigration Time of Sucralfate is 2.02±0.157 in Stomach medium and F.L.T of Metoproplol Succinate is 785 sec and T.F.T is >20 hours.[T-25].

11-Accelerated Stability study and in vitro evaluation of SFMS Bilayered Floating Tablet at different time period
Physical properties like weight variation, thickness, hardness, % friability, disintegration time of SF layer, FLT and TFT of Bilayed floating tablet shows near about equivalent parameters as initial post compresional parameters.[T26].

12-In vivo evaluation
The X-ray photographs of in vivo floating efficacy of floating tablet at different time intervals in rabbit's stomach are shown in Figure12and13. Figure13 shows X-ray before administration (0 hour) of floating tablet. Floating tablet can be seen in the stomach. Next image, Figure 13A, taken at 1 hour shows change in position of floating tablet; this shows that floating tablet did not adhere to gastric mucous. Next image, Figure 13B and 12C, taken at 2 h and 4 h after administration of floating tablet showed that floating tablet was still found tobe buoyant on gastric content, respectively. At figure 12D, taken at 6h after administration of floating tablet showed that floating tablet at lower gastric region displayed still buoyant position.

The in vivo (X-Ray) evaluation of floating tablets showed that the tablet was floating in the rabbit stomach up to 6 hours.

Table 1: List of excipients used for the preparation of Sucralfate layer.

Sl. No.	Excipient name	Category
1	Crosspovidone	Tablet Disintegrant
2	MCC PH101	Tablet Filler/ Diluent
3	Lactose monohydrate (Flowlac)	Tablet Filler/ Diluent
4	Sodium bicarbonate	Alkalizing Agent
5	Calcium carbonate	Buffering Agent
6	Aerosil/ colloidal SiO2	Tablet Disintegrant
7	Hydroxypropylcellulose	Tablet Binder
8	Sodiumlaurylsulfate	Solubilizer
9	Polysorbate 80	Solubilizer
10	Magnesium Stearate	Tablet lubricant
11	Sunset Yellow	Coloring agent

Table 2: List of excipients used for the preparation of Metoprolol Succinate.

Sl. No	Excipient Name	Category
1	HPMCK100M	Swellable polymer
2	Ethyl cellulose	Drug release retardant
3	HPC Klucel HF	Matrix former
4	PovidoneK90	Matrix Former
5	Sodium Alginate	Swellable Polymer
6	NaCMC	Swellable polymer
7	Eudragit polymers	Swellable polymer
8	Aerosil/ colloidal SiO2	Anti-caking agent
9	Talc	Tablet Glidant
10	Isopropyl alcohol (IPA)	Solvent
11	Purified water	Granulating fluid

Table 3: Standard graph of Sucralfate in 6.8 pH Phosphate buffer at 281nm.

Concentration (µg/ml)	Absorbance at 281nm
0	0
5	0.1693±0.0003
10	0.3570±0.0004
15	0.5505±0.0003
20	0.7412±0.0002
25	0.9463±0.0003
R^2	0.999

Table 4: Standard graph of Sucralfate in 0.1N HCl at 281nm.

Concentration (µg/ml)	Absorbance at 281nm
0	0.0000
5	0.1861±0.0002
10	0.3739±0.0004
15	0.5605±0.0002
20	0.7543±0.0003
25	0.9454±0.0002
R^2	0.999

Table 5: Standard curve of Metoprolol Succinate in 0.1N HCl at 233nm.

Concentration (µg/ml)	Absorbance at 233 nm
0	0.0000
5	0.2439±0.0002
10	0.4235±0.0003
15	0.6458±0.0001
20	0.8355±0.0002
25	1.0684±0.0003
R^2	0.998

Table 6: Flow properties of Sucralfate.

Sl. No.	Parameter	Observation
1.	Bulk Density (g/ml)	0.308
2.	Tapped Density (g/ml)	0.554
3.	Carr's Index (%)	44.40
4.	Hausner's Ratio	1.798
5.	Angle of Repose (Θ)	65.00
6.	Result	Poor

Table 7: Flow properties of Metoprolol Succinate.

Sl. No.	Parameter	Observation
1.	Bulk Density (g/ml)	0.707
2.	Tapped Density (g/ml)	0.838
3.	Carr's Index (%)	15.63
4.	Hausner's Ratio	1.185
5.	Angle of Repose (Θ)	28.52
6.	Result	Good Flow

Table 8: Composition of Sucralfate Tablets.

	Ingredients	Quantity per tablet in MG								
		SF 1	SF 2	SF 3	SF 4	SF 5	SF 6	SF 7	SF 8	SF 9
1	Sucralfate	100	100	100	100	100	100	100	100	100
2	Crospovidone	0	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25
3	Calcium carbonate	23	25	25	25	0	25	0	0	0
4	Aerosil	1	1	1	1	1	1	1	1	1
5	Lactose MHF	31.25	31.25	31.25	31.25	31.25	31.25	31.25	31.25	31.25
6	MCC PH 101	48.45	45.2	44.575	44.575	74.575	49.575	49.575	49.825	46.075
7	Magnesium Stearate	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
8	Sodium bicarbonate	5	5	5	5	0	0	25	25	25
9	Polysorbate 80	0	0	0	0.625	0.625	0.625	0.625	0.375	0.375

10	SLS	0	0	0.625	0	0	0	0	0	0
11	Sunset yellow	0.312	0.3125	0.3125	0.3125	0.3125	0.3125	0.3125	0.3125	0.3125
12	Purified Water	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
	Total wt of Tablet	214.5	214.5	214.5	214.5	214.5	214.5	214.5	214.5	214.5

Table 9: Composition of Sucralfate tablets subjected to optimization studies.

Sl No	Ingredients	Quantity per tablet in MG					
		SF 10	SF 11	SF12	SF 13	SF 14	SF 15
1	Sucralfate	100	100	100	100	100	100
2	Crospovidone	6.25	6.25	3.75	8.75	6.25	6.25
3	Aerosil	1	1	1	1	1	1
4	Lactose MFL	31.25	31.25	31.25	31.25	31.25	31.25
5	MCC PH101	48.575	43.575	48.575	43.575	52.325	39.825
6	Magnesium Stearate	0.5	0.5	0.5	0.5	0.5	0.5
7	Sodium Bicarbonate	25	25	25	25	18.75	31.25
8	Polysorbate 80	0.375	0.375	0.375	0.375	0.375	0.375
9	HPC-L	1.25	6.25	3.75	3.75	3.75	3.75
10	Sunset Yellow	0.3125	0.3125	0.3125	0.3125	0.3125	0.3125
11	Purified Water	q.s	q.s	q.s	q.s	q.s	q.s
	Total Weight	214.5	214.5	214.5	214.5	214.5	214.5

Table 10: Composition of floating SR Metoprolol Succinate tablets.

Sl. No	Ingredients	Quantity per tablet in MG									
		F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
1	Metoprolol Succinate	50	50	50	50	50	50	50	50	50	50
2	HPMC K 100M	100	100	100	100	100	100	100	100	100	75
3	SODIUM BICARBONATE	75	100	100	100	100	100	100	100	100	100
4	AEROSIL	3	3	3	3	3	3	3	3	3	3
6	EUDRAGIT RSPO	30	30	-		-	-	-	-	-	30
7	EUDRAGIT RLPO	-	-	30		-	-	-	-	-	-
8	EUDRAGIT RS100	-	-		30	-	-	-	-	-	-
8	Na CMC	-	-	-	-	30	-	-	-	-	-
9	SODIUM ALGINATE	-	-	-	-		30	-	-	-	-
10	HPC KLUCEL HF	-	-	-	-	-	-	30	-	-	-
11	PVPK 90	-	-	-	-	-	-	-	30	-	-
12	ETHYL CELLULOSE	-	-	-	-	-	-	-	-	30	-
13	TALC	3	3	3	3	3	3	3	3	3	3
14	IPA	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
15	PURIFIED WATER	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
	TOTAL WEIGHT	261	286	286	286	286	286	286	286	286	261

Table 11: Flow properties of lubricated granules of Sucralfate.

Formulation Code	Angle of Repose (Ɵ)	Bulk Density (g/ml)	Tapped Density (g/ml)	Compressibility Index (%)	Hausner's Ratio	%LOD
SF1	27.53	0.507	0.687	26.20	1.314	2.13
SF2	27.82	0.521	0.622	21.31	1.248	2.86
SF3	26.27	0.546	0.694	21.33	1.254	2.68
SF4	25.43	0.454	0.547	17.17	1.186	2.26
SF5	26.13	0.503	0.629	20.03	1.264	2.28
SF6	25.52	0.506	0.634	20.19	1.257	2.74
SF7	26.19	0.502	0.609	17.57	1.229	2.78
SF8	26.33	0.526	0.676	22.25	1.229	2.92
SF9	26.23	0.501	0.615	18.54	1.310	2.73
SF10	26.28	0.500	0.627	20.25	1.263	2.78
SF11	26.31	0.507	0.625	18.88	1.239	2.91
SF12	26.48	0.505	0.623	18.94	1.221	2.64

SF13	16.06	0.511	0.624	22.11	1.284	2.68
SF14	25.73	0.505	0.616	18.02	1.229	2.89
SF15	26.33	0.511	0.620	17.58	1.212	2.77

Table 12: Flow properties of lubricated granules of Metoprolol Succinate.

Formulation Code	Angle of Repose (Θ)	Bulk Density (g/ml)	Tapped Density (g/ml)	Compressibility Index (%)	Hausner's Ratio	% LOD
MSF1	31.36	0.374	0.531	29.56	1.419	1.74
MSF2	22.53	0.343	0.514	33.26	1.498	1.89
MSF3	32.72	0.368	0.508	27.55	1.380	1.93
MSF4	32.39	0.348	0.492	29.26	1.475	1.83
MSF5	32.66	0.341	0.503	32.20	1.475	1.79
MSF6	32.73	0.356	0.502	29.08	1.410	1.87
MSF7	32.61	0.342	0.479	28.60	1.400	1.92
MSF8	32.53	0.353	0.497	28.97	1.407	1.90
MSF9	33.04	0.359	0.509	29.46	1.417	1.76
MSF10	32.44	0.331	0.481	31.18	1.453	1.96

Table 13: Accelerated Stability Study of Sucralfate Lubricated Granules.

Granules	After 7 Days	After 15 Days	After 30 Days	After 45 Days	After 60 Days	After 90 Days
SF1	No Change	No Change	No Change	No Change	No Change	Slide yellowish
SF2	No Change	No Change	No Change	No Change	No Change	Rare black spots
SF3	No Change	No Change	No Change	No Change	No Change	Started melting
SF4	No Change	No Change	No Change	No Change	No Change	Odour change
SF5	No Change	No Change	No Change	No Change	No Change	Agglomeration
SF6	No Change	No Change	No Change	No Change	No Change	Started caking
SF7	No Change	No Change	No Change	No Change	No Change	Rare black spot
SF8	No Change	No Change	No Change	No Change	No Change	Odour change
SF9	No Change	No Change	No Change	No Change	No Change	Stick at the wall
SF10	No Change	No Change	No Change	No Change	No Change	Less flowibility
SF11	No Change	No Change	No Change	No Change	No Change	Rare black spot
SF12	No Change	No Change	No Change	No Change	No Change	Slide yellowish
SF13	No Change	No Change	No Change	No Change	No Change	No change
SF14	No Change	No Change	No Change	No Change	No Change	Rare black spot
SF15	No Change	No Change	No Change	No Change	No Change	Slide yellowish

Table 14: Accelerated Stability Study of Sucralfate Lubricated Granules.

Granules	After 7 Days	After 15 Days	After 30 Days	After 45 Days	After 60 Days	After 90 Days
MSF1	No Change	No Change	No Change	No Change	No Change	Odour change
MSF2	No Change	No Change	No Change	No Change	No Change	No change
MSF3	No Change	No Change	No Change	No Change	No Change	Slide yellowish
MSF4	No Change	No Change	No Change	No Change	No Change	Odour change
MSF5	No Change	No Change	No Change	No Change	No Change	Rare black spot
MSF6	No Change	No Change	No Change	No Change	No Change	Slide yellowish
MSF7	No Change	No Change	No Change	No Change	No Change	Rare black spot
MSF8	No Change	No Change	No Change	No Change	No Change	Started melting
MSF9	No Change	No Change	No Change	No Change	No Change	Stick at the wall
MSF10	No Change	No Change	No Change	No Change	No Change	Rare black spot

Table 15: Flow properties of lubricated granules of Sucralfate after 90 days of Accelerated Stability Study.

Formulation Code	Angle of Repose (Θ)	Bulk Density (g/ml)	Tapped Density (g/ml)	Compressibility Index (%)	Hausner's Ratio	% LOD
SF1	27.93	0.607	0.598	24.12	1.567	2.45
SF2	26.82	0.531	0.602	23.52	1.835	2.74
SF3	35.27	0.934	0.701	19.53	1.932	2.58
SF4	25.43	0.326	0.589	16.20	1.682	2.19

SF5	38.03	0.723	0.624	19.10	1.257	2.18
SF6	42.42	0.499	0.599	21.16	1.326	2.92
SF7	30.19	0.513	0.601	18.57	1.432	2.67
SF8	26.43	0.612	0.654	24.16	1.159	2.89
SF9	46.23	0.857	0.624	19.64	1.452	2.45
SF10	48.28	0.802	0.635	21.20	1.321	2.61
SF11	26.41	0.359	0.667	17.57	1.238	2.89
SF12	26.58	0.550	0.645	14.72	1.543	2.58
SF13	22.06	0.511	0.632	19.22	1.427	2.47
SF14	26:73	0.498	0.652	20.03	1.248	2.79
SF15	28.33	0.502	0.612	18.74	1.198	2.65

Table 16: Flow properties of lubricated granules of Metoprolol Succinate after 90 days of Accelerated Stability Study.

Formulation Code	Angle of Repose (Θ)	Bulk Density (g/ml)	Tapped Density (g/ml)	Compressibility Index (%)	Hausner's Ratio	% LOD
F1	32.36	0.325	0.501	24.31	1.398	1.82
F2	20.53	0.512	0.498	28.26	1.504	1.67
F3	36.72	0.298	0.499	24.32	1.471	1.54
F4	32.39	0.334	0.467	27.14	1.571	1.91
F5	34.66	0.421	0.518	29.32	1.672	1.63
F6	34.73	0.352	0.525	32.14	1.534	1.68
F7	33.61	0.299	0.489	31.11	1.398	1.89
F8	51.53	0.504	0.501	28.10	1.399	1.88
F9	48.04	0.502	0.498	30.39	1.418	1.91
F10	32.54	0.341	0.479	29.21	1.445	1.99

Table 17: Post compressional parameters of the formulated Sucralfate tablets.

Formulation Code	Average weight (mg)	Thickness (mm)	Hardness (KP)	% Friability	Disintegration Time (min)	% Drug Content
SF1	214.1±0.517	3.24±0.010	5.75±0.088	0.239	24.46±0.579	98.88
SF2	212.6±0.632	3.53±0.008	5.87±0.214	0.239	5.21±0.079	99.33
SF3	216.8±0.707	3.18±0.021	5.62±0.370	0.159	14.16±0.497	100.73
SF4	209.2±0.441	3.18±0.024	5.51±0.228	0.398	0.46±0.690	99.57
SF5	211.4±0.601	3.04±0.036	5.68±0.130	0.079	9.28±0.132	98.15
SF6	208.3±0.500	3.17±0.008	5.78±0.116	0.238	6.28±0.043	100.46
SF7	214.8±0.632	3.53±0.06	5.91±0.216	0.318	6.29±0.047	99.95
SF8	216.6±0.440	3.29±0.026	5.87±0.386	0.397	6.56±0.046	99.69
SF9	211.2±0.500	3.19±0.010	5.97±0.179	0.316	1.3±0.066	100.14
SF10	218.5±0.527	3.01±0.021	5.81±0.116	0.396	1.22±0.115	100.56
SF11	215.2±0.737	3.19±0.038	6.15±0.263	0.317	23.96±0.853	100.3
SF12	209.1±0.500	3.03±0.016	5.64±0.357	0.238	8.2±0.123	99.62
SF13	218.2±0.500	3.08±0.012	6.11±0.187	0.079	0.51±0.079	99.15
SF14	213.1±0.440	3.05±0.014	5.28±0.116	0.317	5.23±0.023	100.15
SF15	215.1±0.462	3.09±0.019	5.58±0.203	0.158	2.28±0.016	99.24

Table 18: Post compressional parameters of the formulated Metoprolol Succinate Tablets.

Formulation Code	Average weight(mg)	Thickness (mm)	Hardness (KP)	% Friability	% Drug content	FLT (SEC)	TFT (HR)
MSF1	260.7±0.500	3.14±0.015	7.75±0.105	0.163	98.58	18	>20
MSF2	283.8±0.527	3.28±0.009	8.87±0.138	0.092	101.61	16	>20
MSF3	281.4±0.707	3.28±0.010	8.77±0.115	0.144	101.87	27	>20
MSF4	279.3±0.881	3.29±0.010	7.86±0.091	0.145	98.22	30	>20
MSF5	281.0.±0.500	3.25±0.014	8.86±0.121	0.131	100.65	18	>20
MSF6	283.9±0.527	3.29±0.007	8.71±0.147	0.197	100.91	28	>20
MSF7	281.2±0.707	3.28±0.019	8.87±0.150	0.105	100.83	27	>20

MSF8	283.8±0.527	3.28±0.011	8.87±0.076	0.183	98.65	30	>20
MSF9	280.4±0.667	3.27±0.030	7.8±0.089	0.105	99.88	53	>20
MSF10	282.8±0.632	3.64±0.036	8.62±0.179	0.136	99.59	21	>20

Table 19: Swelling index values observed from Metoprolol Succinate tablets.

Time (HR)	% Swelling									
	MSF1	MSF2	MSF3	MSF4	MSF5	MSF6	MSF7	MSF8	MSF9	MSF10
0	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
1	85.72	96.0	83.5	82.7	105.7	114.2	71.1	110.2	68.9	83.9
2	92.96	113.7	106.1	108.1	128.0	160.4	100.5	152.7	102.6	111.6
3	149.2	153.5	147.6	148.4	155.5	187.4	149.2	181.3	129.5	122.0
4	160.8	165.3	164.7	173.7	178.6	197.0	153.5	199.9	138.4	148.4
5	171.9	188.6	184.3	188.5	193.3	216.1	164.5	209.9	150.3	176.1
6	194.3	190.2	190.3	189.7	200.1	226.7	184.2	222.5	171.5	180.4
7	201.2	203.1	202.0	202.6	209.9	239.8	191.4	237.1	177.5	200.3
8	214.1	215.0	210.5	209.2	212.4	214.3	211.2	242.7	187.4	208.9

Table 20: Accelerated Stability Study of Sucralfate Tablet.

Tablets	After 7 Days	After 15 Days	After 30 Days	After 45 Days	After 60 Days	After 90 Days
SF1	No Change	No Change	No Change	No Change	No Change	Slide yellowish
SF2	No Change	No Change	No Change	No Change	No Change	Rare black spots
SF3	No Change	No Change	No Change	No Change	No Change	No change
SF4	No Change	No Change	No Change	No Change	No Change	No Change
SF5	No Change	No Change	No Change	No Change	No Change	Rare black spot
SF6	No Change	No Change	No Change	No Change	No Change	No change
SF7	No Change	No Change	No Change	No Change	No Change	Rare black spot
SF8	No Change	No Change	No Change	No Change	No Change	No change
SF9	No Change	No Change	No Change	No Change	No Change	No change
SF10	No Change	No Change	No Change	No Change	No Change	No change
SF11	No Change	No Change	No Change	No Change	No Change	Rare black spot
SF12	No Change	No Change	No Change	No Change	No Change	Slide yellowish
SF13	No Change	No Change	No Change	No Change	No Change	No change
SF14	No Change	No Change	No Change	No Change	No Change	Rare black spot
SF15	No Change	No Change	No Change	No Change	No Change	No change

Table 21: Accelerated Stability Study of Metoprolol Succinate Tablet.

Tablets	After 7 Days	After 15 Days	After 30 Days	After 45 Days	After 60 Days	After 90 Days
Msf1	No Change	No Change	No Change	No Change	No Change	No Change
Msf2	No Change	No Change	No Change	No Change	No Change	No Change
Msf3	No Change	No Change	No Change	No Change	No Change	Slide Yellowish
Msf4	No Change	No Change	No Change	No Change	No Change	No Change
Msf5	No Change	No Change	No Change	No Change	No Change	Rare Black Spot
Msf6	No Change	No Change	No Change	No Change	No Change	No Change
Msf7	No Change	No Change	No Change	No Change	No Change	Rare Black Spot
Msf8	No Change	No Change	No Change	No Change	No Change	No Change
Msf9	No Change	No Change	No Change	No Change	No Change	No Change
Msf10	No Change	No Change	No Change	No Change	No Change	Rare Black Spot

Table 22: Composition of optimized Sucralfate layer in SFMS tablets.

SL. No	Ingredients of SF 9	Quantity Per Tablet in mg
1	SUCRALFATE	100
2	CROSS POVIDONE	6.25
3	AEROSIL	1
4	LMFL	31.25
5	MCC PH101	46.075

6	SBC	25
7	POLYSORBATE 80	0.375
8	HPC-L	3.75
9	MAGNESIUM STEARATE	0.5
10	SUNSET YELLOW (0.25%)	0.3125
11	PURIFIED WATER	q.s
	TOTAL WEIGHT	214.5

Table 23: Composition of optimized Metoprolol Succinate layer in SFMS tablets.

Sl.no	Ingredients	Quantity per tablet in mg
1	METOPROLOL	50
2	HPMC K 100M	100
3	SBC	100
4	AEROSIL	3
5	EUDRAGIT RSPO	30
6	TALC	3
7	IPA	Q.S
8	PURIFIED WATER	Q.S
	TOTAL WEIGHT	286

Table 24: Accelerated Stability Study of granules of Sucralfate and Metoprolol Succinate of selected formulations.

Granules	After 7 Days	After 15 Days	After 30 Days	After 45 Days	After 60 Days	After 90 Days
SF13	No Change	No Change	No Change	No Change	No Change	No Change
MS2	No Change	No Change	No Change	No Change	No Change	No Change

Table 25: Post compressional parameters observed from the bilayered tablets of SFMS.

SL. No.	Parameter	Observed Value
1	Average Weight (mg)	494.7±0.866
2	Thickness (mm)	5.89±0.136
3	Hardness (KP)	8.3±0.348
4	% Friability	0.646
5	FLT (sec)	785
6	TFT (hr)	>20
7	DT of sucralfate layer	2.02±0.157

Table 26: Accelerated Stability Study and in vitro evaluation of Bi -layer Floating Tablet of Sucralfate and Metoprolol Succinate at different time period.

Sl No	Parameters	Observed Value	After 15 Days	After 30 Days	After 60 Days	After 90 Days
1	Average Weight(mg)	494.7±0.86	472.1±0.26	485.7±0.46	462.7±0.57	448.7±0.37
2	Thickness(mm)	5.89±0.136	6.10.±0.025	5.92.034	5.89±0.156	5.91±0.252
3	Hardness (KP)	8.3±0.394	8.3±0.159	8.3±0.832	8.3±0.752	8.3±0.659
4	% Friability	0.646	0.798	0.842	0.912	0.886
5	DT of Sucralfate layer	2.02±0.10	2.02±0.21	2.02±0.42	2.02±0.68	2.02±0.59
6	TFT(hr) of MS	>20	>20	>20	>20	>20
7	FLT(SEC)of MS	785	805	789	799	802

DT- Disintegration Time TFT-Total floating Time FLT- Floating lag Time

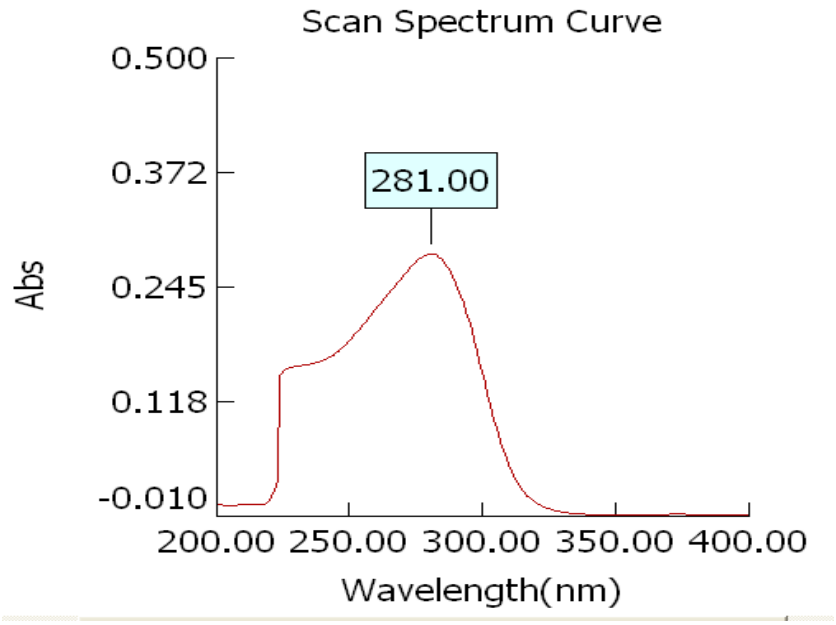

Fig 1: Scanned spectra of Sucralfate.

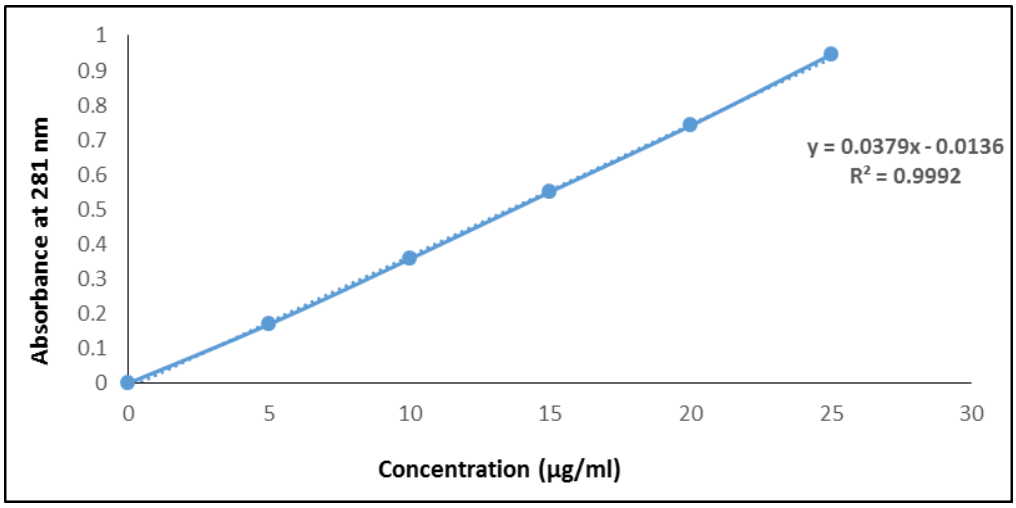

Fig 2: Calibration curve of Sucralfate in 6.8pH phosphate buffer at 281nm.

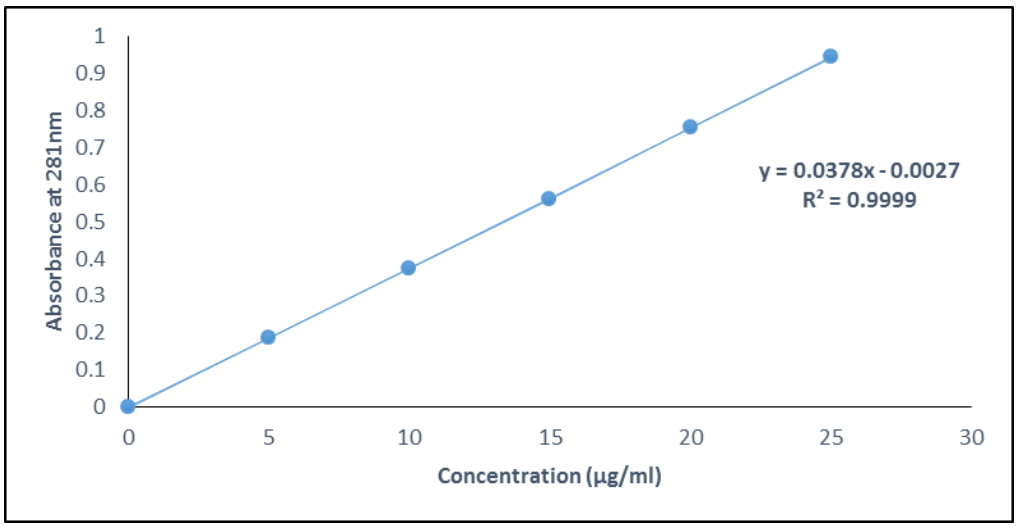

Fig 3: Calibration curve of Sucralfate in 0.1N HCl at 281nm.

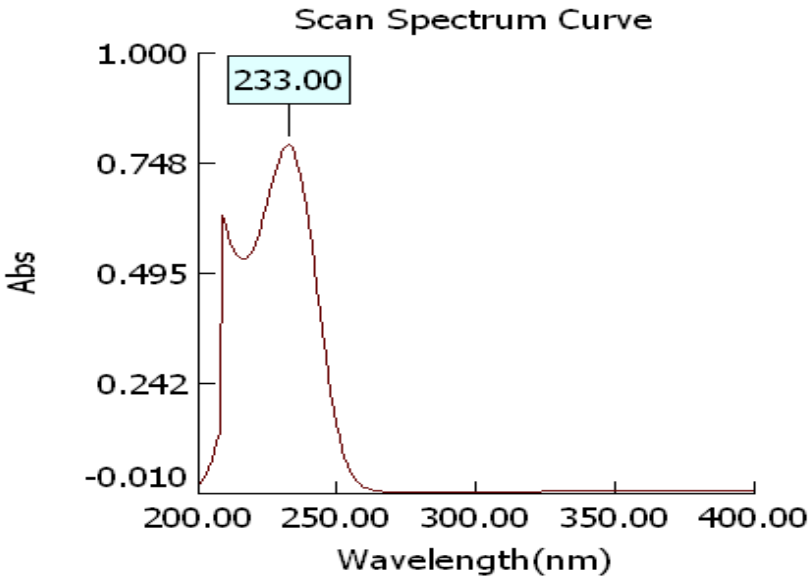

Fig. 4: Scanned spectra of Metoprolol Succinate.

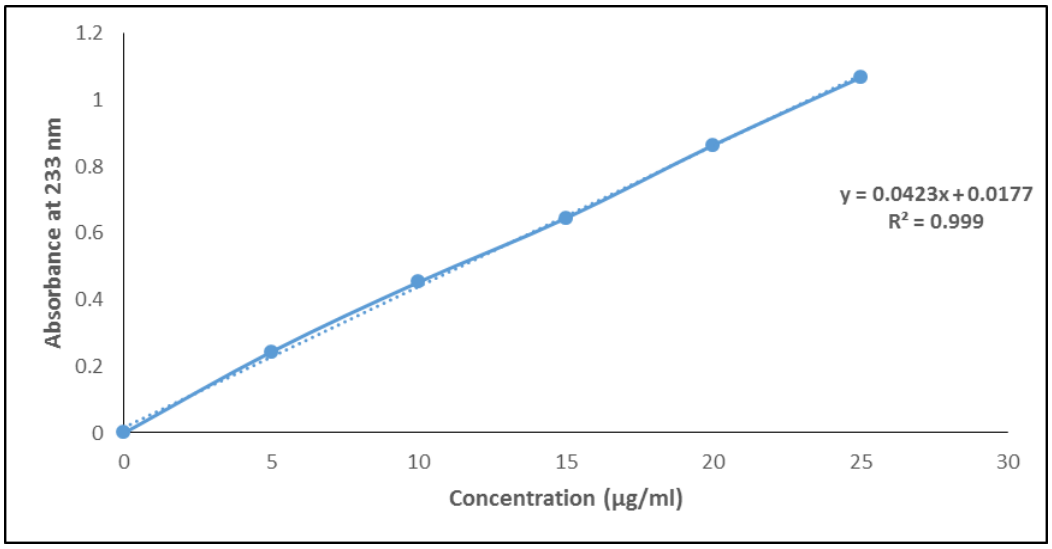

Fig 5: Calibration curve of Metoprolol Succinate in 6.8pH phosphate buffer at 233nm.

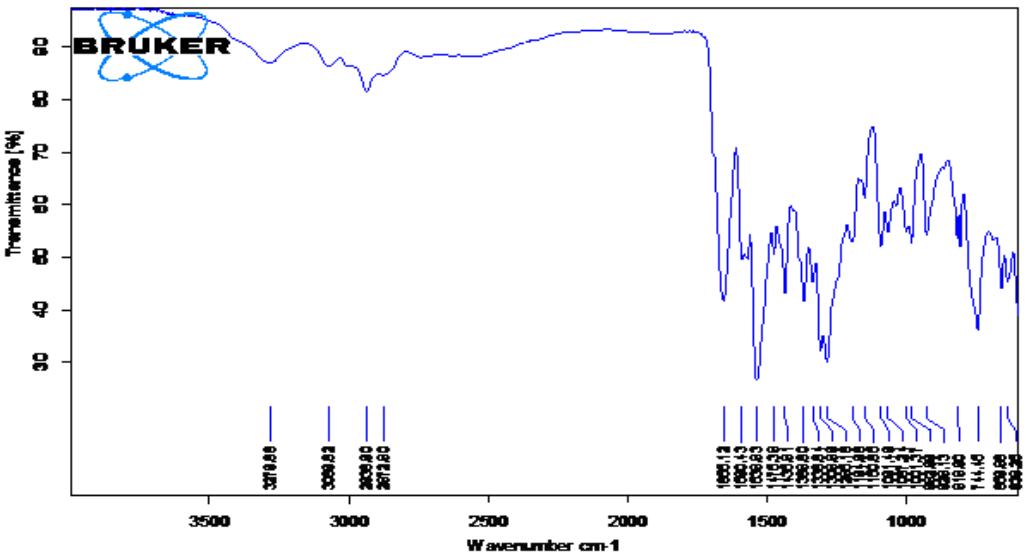

Figure 6: IR spectra of Pure drug of Sucralfate.

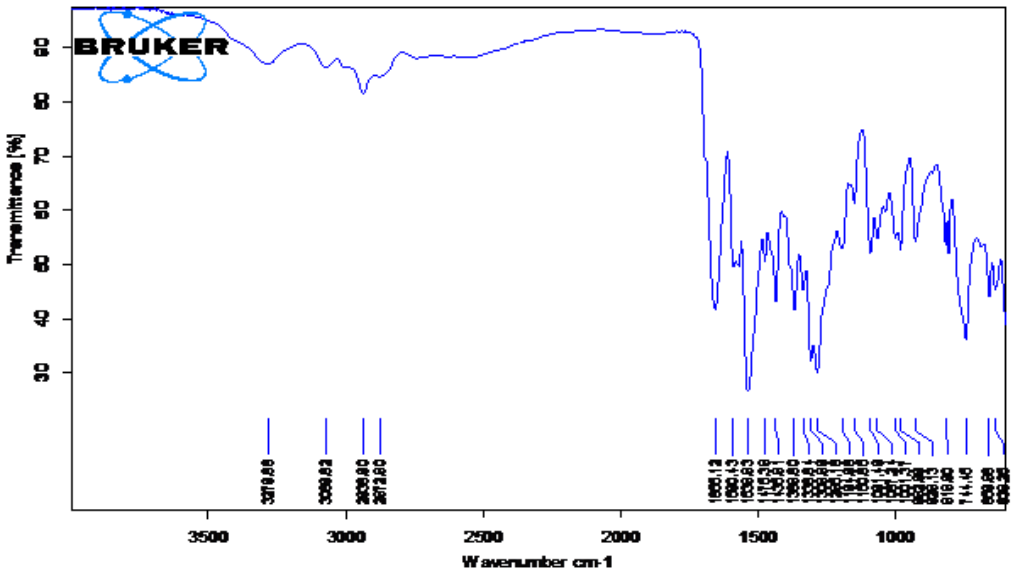

Figure 7: IR spectra of Pure drug Metoprolol Succinate

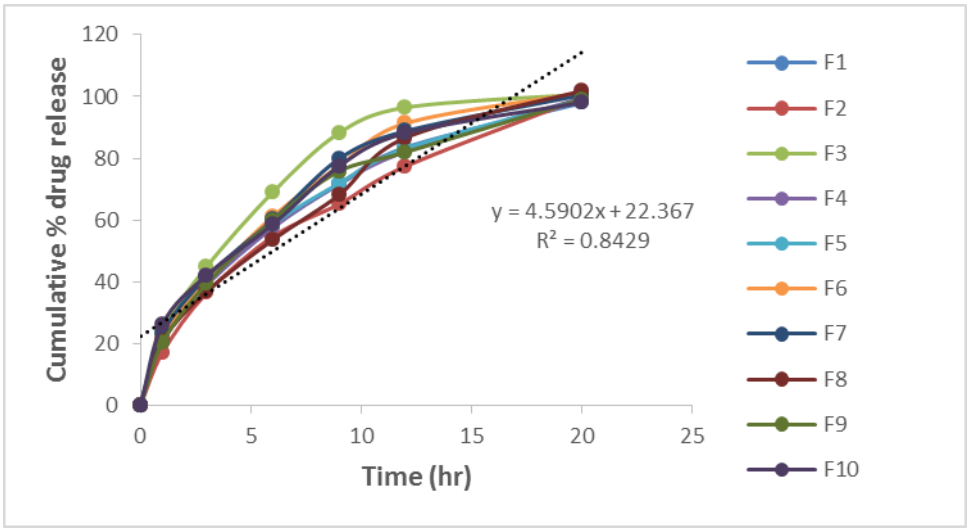

Fig. 8: Zero order plots of Metoprolol Succinate formulations containing different polymer concentrations.

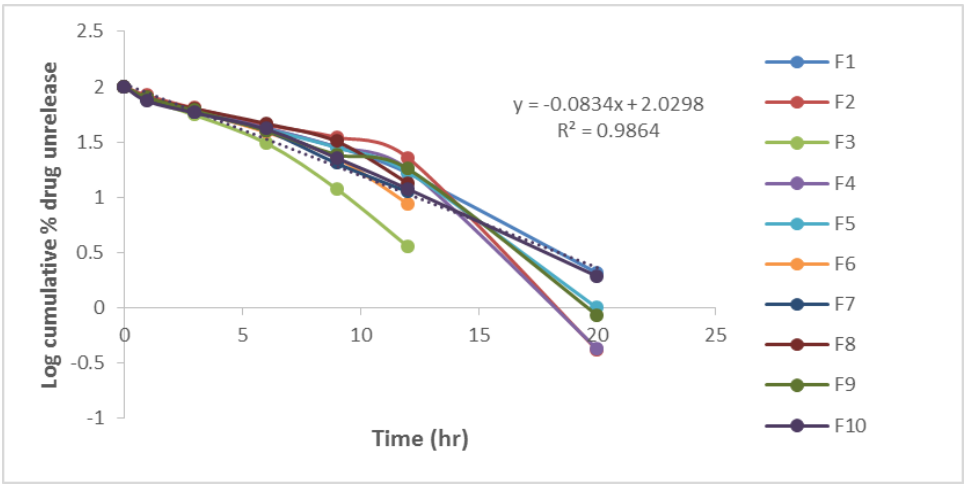

Fig 9: First order plots of Metoprolol Succinate formulations containing different polymer concentration.

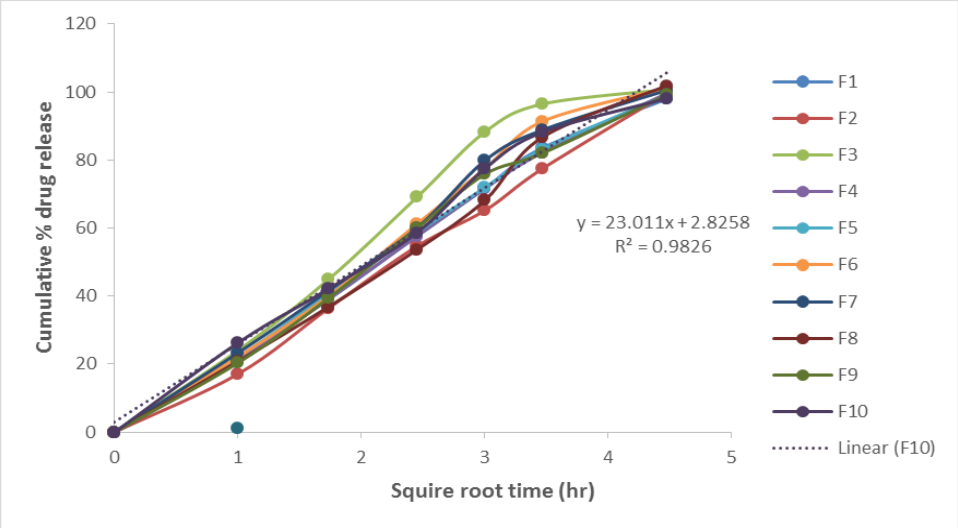

Fig 10: Higuchi plots of Metoprolol Succinate from formulations containing different polymers.

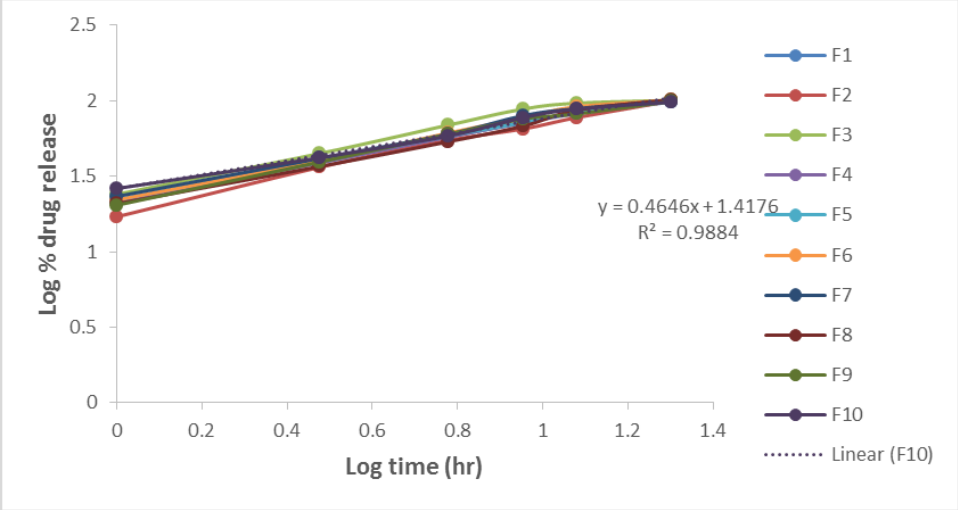

Fig 11: Pappas plots of Metoprolol Succinate from formulations containing different polymers.

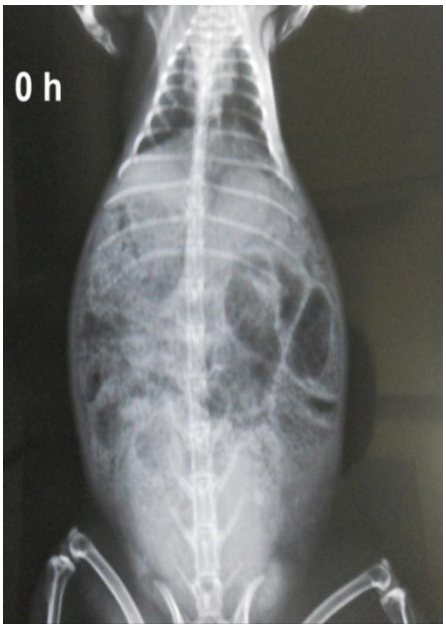

Figure 12: X-ray photograph of rabbit before treatment (0 hour, before tablet administration) from abdomen portion (Control).

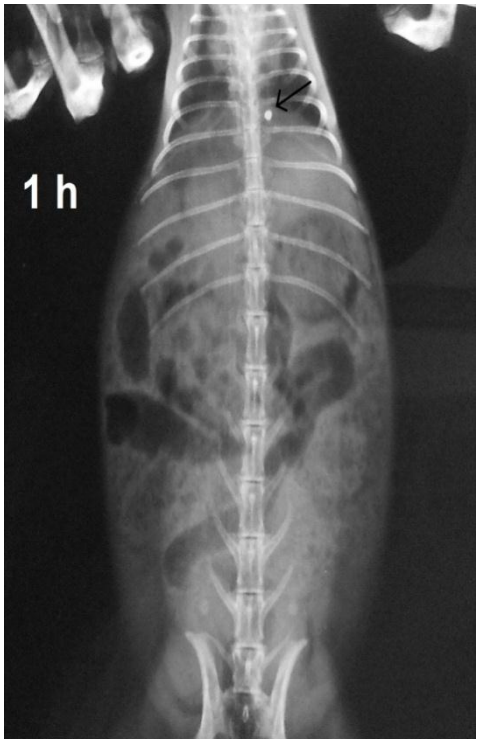

Figure: 13A

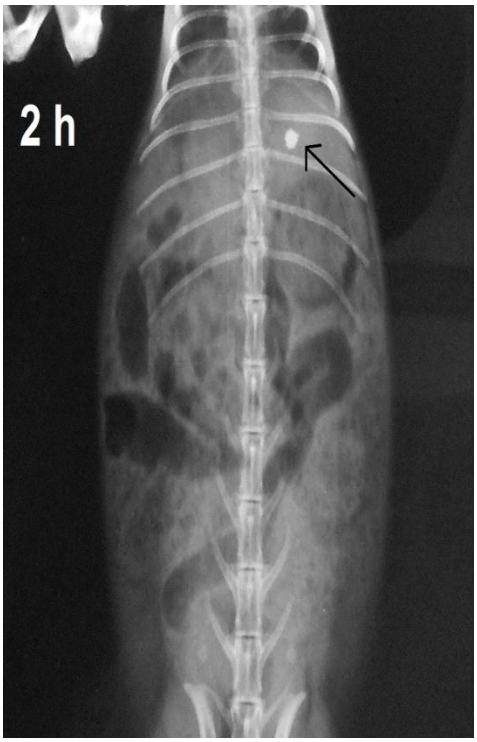

Figure: 13B

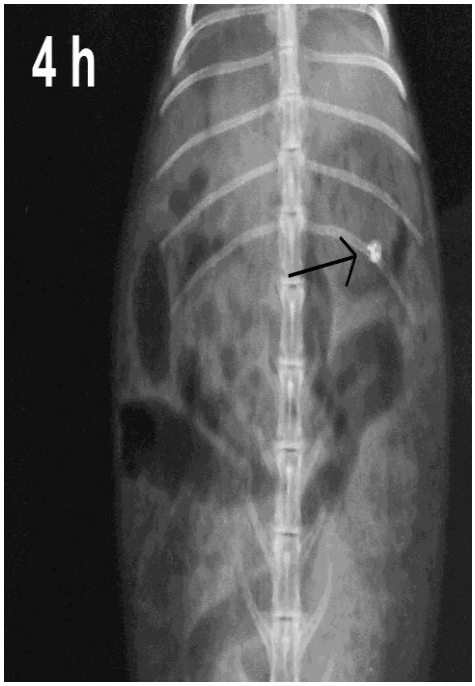

Figure: 13C

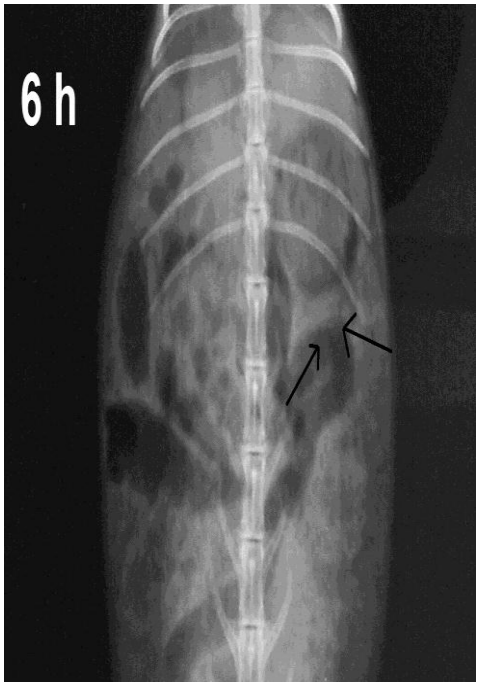

Figure: 13D

Figure 13: X-ray photograph of rabbit after treatment at specified time intervals from abdomen portion (Control).

CONCLUSIONS

The result of present study indicate that after various types of in vitro and in vivo evaluation from 15 formulations of Sucralfate and 10 formulations of Metoprol Succinate, the combination of formulations (SF13 and MSF2) provide the better properties of Bi layer floating tablet. The present study can generate a new scope in optimization of formulations and clinical trials and can produce better identification in Gastro Retentive Drug Delivery System.

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