FORMULATION AND EVALUATION OF FLOATING TABLETS OF OXAMNIQUINE

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ABSTRACT

While chemotherapeutic drugs, such as praziquantel, oxamniquine and metrifonate, are currently considered safe and effective drugs for schistosomiasis treatment, reinfection occurs frequently after drug treatment. Thus, an attempt has been made in the present study to produce floating tablets of Oxamniquine. The polymers tragacanth, guar gum, xanthan gum, and microcrystalline cellulose, along with an effervescent base of sodium bicarbonate, were used to make Oxamniquine floating tablets (400 mg). The presence of any drug/polymer/excipients interactions was confirmed by an FTIR investigation. The results confirmed as Hardness 3.4 to 4.0kg/cm2 weight fluctuation, thickness, friability 0.70 to 0.87, drug content 90.00 to 99.90%, floating lag time, and in vitro dissolution investigations were all performed on the manufactured floating tablets. B1, B2, B4, B5, B7, and B8 were the only eight formulationsthat showed satisfactory floating properties. And all pill formulations have good evaluation properties.

Key words: Oxamniquine, floating tablet, tragacanth, guar gum, xanthan gum.

INTRODUCTION:

As a primary prevention of transmission, the therapy consists of treating the disease, lowering the parasite burden of the host, preventing the disease from progressing to a severe stage, and minimizing the production and deposition of helminthic eggs in the environment. The medication therapy of schistosomiasis is similar to that of other parasitic diseases, but it has always been hampered by the difficulties in identifying chemotherapeutic drugs with high effectiveness and tolerance. At first, trivalent antimony compounds such as emetic tartar (potassium antimony tartrate) were used [1] Schistosomiasis is a parasitic illness spread by the trematode worms of the genus Schistosoma. According to the UNHCO, about 250 million people worldwide are infected, with an additional 700 million at risk in 74 countries where the illness is prevalent. The illness kills around 200,000 people in Sub-Saharan Africa each year.[2] Current schistosomiasis treatment and prevention rely solely on two medications, oxamniquine and Oxamniquine. Oxamniquine is a prodrug that is exclusively used against S. mansion when Oxamniquine treatment fails. Oxamniquine is active because of DNA binding, however it only targets adult parasites and can infrequently cause major adverse effects.[3] Human schistosomiasis, one of the most common neglected tropical diseases, is a serious public health issue that affects over 200 million people in 78 countries, with an additional 800 million people at risk of infection.[4] Although schistosomiasis fatality statistics are difficult to quantify, it is believed that this illness kills roughly 280,000 people each year and can still inflict substantial harm to the host.[5] It is a helminthiasis caused by an intravascular trematode of the Schistosoma genus, with three primary species capable of infecting humans: Schistosoma haematobium, S. mansion, and S. japonicum. Disease spread is aided by poor hygienic conditions as well as a lack of economic growth. Adult versions of this parasite live in numerous sites in the vertebrate host's mesenteric arteries.[6] Schistosomiasis is a worldwide illness that mostly affects nations in Sub-Saharan Africa, as well as some portions of Asia and South America. An estimated 779 million individuals are at risk of infection, with children accounting for more than half of those at risk. Over 200 million individuals have been affected.[7] There is no vaccination, and the only medicine approved for the treatment of Schistosoma spp. infections is Oxamniquine. Worryingly, the schistosomiasis medication pipeline is depleted. Oxamniquine is a medication that is often used in mass drug administration (MDA), also known as preventative chemotherapy.[8]

In Sub-Saharan Africa, for example, around 89 million doses of Oxamniquine were delivered in 2016. However, it is not an ideal medication, owing to its limited potency against juvenile Schistosoma spp. stages and considerable inter-individual heterogeneity of effects.[9] The convenient and favorite means of delivery of drugs to the systemic circulation is the oral administration. Recently, orally controlled release pharmaceutical products have become increasingly important in achieving improved therapeutic benefits like easy dosing of patients' compliance and formulation flexibility. Drugs which are quickly removed from systems circulation from the gastrointestinal tract and have a short half-live. In order to achieve appropriate treatment activity, frequent dosing of these medicines is necessary. The development of orally continuous-controlled release formulations is an attempt to liberate the drug into the gastrointestinal tract slowly, thus maintaining a long-term efficient drug concentration in the systemic circulation [10]

MATERIALS AND METHODS:

Oxamniquine were received from Pure chem,Gujarat. Tragacanth, Guar gum, Talc, Microcrystalline cellulose, Sodium bicarbonate, polyvinylpolypyrrolidone and Magnesium stearate were obtained from Yarrow chem Mumbai, Central drug houseNew Delhi, Hi media Laborotoeies Mumbai, Milo-chem Mumbai, Hualien’s chemicalsMumbai, Milo-chem Mumbai,

Powder pack chem. Mumbai and Milo-chem Mumbai respectively.

Preparation of Floating Tablets:

Oxamniquine floating tablets have been organized by using direct compression. Method using tragacanth, guar gum , xanthan gum,talc,magnesium state, Microcrystalline Cellulose k30,NaHCO3.all the material was collected in mortar and pestle and triturated, to prepare a homogeneous powder and pass in sieve no.60.Magnesium state and talc adding as a lubricant and powder was pressed in rotary tablet Punching machine. [11]

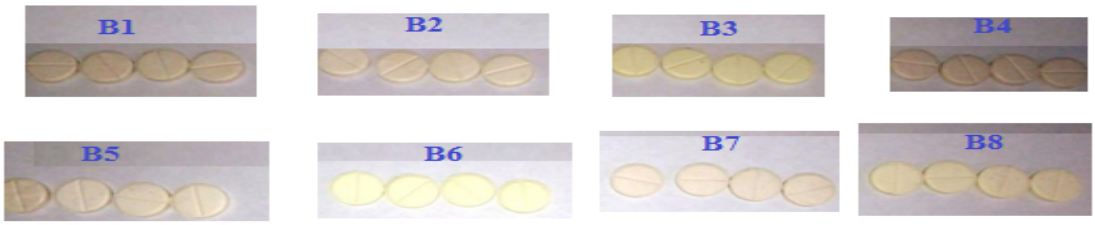


Fig No.1 Prepared Floating Tablets of Oxamniquine

Table No.01 Composition of all Formulation of Prepared Floating Tablets of Oxamniquine

Ingredients	B1	B2	B3	B4	B5	B6	B7	B8
Oxamniquine	100	100	100	100	100	100	100	100
Tragacanth	60	-	-	70	-	-	30	-
Xanthan gum	-	60	-	-	70	-	30	30
Guar gum	-	-	60	-	-	70	-	30
MCC	145	145	145	135	135	135	145	145
Pvpk30	5	5	5	5	5	5	5	5
Na HCO3	74	74	74	74	74	74	74	74
Talc	8	8	8	8	8	8	8	8
Mg. stearate	8	8	8	8	8	8	8	8
Totality.(mg)	400	400	400	400	400	400	400	400

Evaluation of pre compression parameters of powder:

Angle of repose:

The resting angle is a relatively easy method to estimate powder flowability When a funnel isused and the surface free falls and cone and height measured by the application

The angle of rest can be calculated according to the equation.Theta=tan-

1(h/r)

Where, her is the powder cone's relatively high and radius, and mainly rest angle the value for the pharmaceutical product ranges from 25 to 45 and the value is lower. Better flow features [12]

Bulk density & Tapped density:

The mass of powder divided by the bulk volume is known as bulk density. Totally dependson the shape of the particles and the particles become more spherical in form then increase the bulk density. The known quantity of powder, if needed, has been carefully poured into themeasuring cylinder and read into the nearest graduate unit Vee, Unsettled Apparent Volume.

Bulk density = weight of the powder/volume of the packing

Tapped density = weight of the powder/tapped volume of the packing

Car's index [13]

Compressibility index is a useful metric that can be calculated using bulk and tapped densities. According to Car's index, a material with values of less than 20% to 30% is considered free. Flowing material. And it can be calculated as

$$\text{Car's Index (\%)} = \text{TBD} - \text{LBD/TBD} \times 100$$

Hauser's ratio [14]

The Hauser's ratio, which is defined as the ratio of tapped density to bulk density, reveals the flow qualities of the powder.

Evaluation of post compression parameters of tablets:

Thickness[15]

Three pill formulations were chosen at random from each formulation, and thickness was tested individually. And it's measured in millimeters with a standard deviation of was calculated as well. And for using a dial caliper to measure tablet thickness.

Weight variation[15]

Individual weights (WI) OF 20 tablets from each batch were used to evaluate weight variance. Were discovered through the use of an electronic balance. The weight fluctuation was determined with the formula below.

$$\text{\% Weight variation} = (\text{WA-WI})/\text{WA} * 100$$

Hardness [15]

A Pfizer hardness tester was used to determine the hardness of the produced product. For hardness uniformity studies, five floating tablets were prepared. The degree of difficulty is the data was gathered and utilized to calculate the mean, standard deviation, and percent friability. Three tablets were chosen at random and their hardness was assessed.

Friability [15]

The friability of each formulation was tested by taking 20 tablets from each formulation and using the Roche radiator. The machine was turned at a rate of 25 revolutions per minute for 4 minutes. and tablets were removed and reweighted, resulting in a recalculation of the percent friability.

$$\text{\% friability} = (\text{loss in weight/initial weight})*100$$

Drug content uniformity [15]

Three tablets were chosen at random from each batch and carefully weighed and ground in a glass mortar with pestle. 150 mg of medication in a 100 ml volumetric flask containing Ethanol water (1:3) and methanol to make up the remaining volume. And the solution was shaken for 24 hours before being filtered to achieve the necessary dilution. At 263.5 nm, the sample was compared to a blank tablet made in the same way.

In vitro buoyancy studies [15]

All six formulations were subjected to in vitro buoyancy tests using the method described by Rosa et al. Choose pills at random from each formulation and place them in a 100 mL beaker with simulated gastric juice (pH 1.2) according to USP. Floating lag time was defined as the time it took for a tablet to rise and float on a surface. Total floating time refers to how long a dosage form stays afloat on a liquid medium surface.

Swelling index [15]

For each formulation, one tablet was weighed and placed in a beaker containing 200 Maloof distilled water. After each hour, the tablet was taken from the beaker and weighed again.

In vitro dissolution studies [15]

The USP type 1 (basket) Apparatus was used to test Oxamniquine floating tablets. The tablets were placed in jars holding 900 ml of dissolution medium, which was agitated at 10 rpm while maintaining a temperature of 37+0.5. And the jars are filled with buffer pn 1.2 during the first two hours. Following the two-hour jar assembly Jars filled with pn 7.4 buffer solution for period 5 h after that jars filled with pn 9And put at same rpm for 24 hours after that take 1ml were collected.

Drug-polymer interaction by FT-IR [15]

FT-IR formulations 7 and 8 were used to investigate drug and polymer interactions.

Differential scanning calorimetry [15]

Differential scanning calorimetry is used to investigate the purity and impurity of Oxamniquine and polymers such as tragacanth guar gum and xanthan gum. Also, this gives theformulation's physical and energetic qualities.

Stability studies:

The purpose of the stability tests was to see how temperature and relative humidity affected the medication content in various formulations. Formulations were exposed at 400°C with a relative humidity of 75% RH for 24 hours, then sampled and analyzed every day for 90 days.

RESULTS AND DISCUSSION:

Table No.2 Pre-compression parameters of Oxamniquine floating tablet

Formulations	Angle of repose	Bulk density	Tapped density	Car's Index	Hauser's ratio
B1	25.64	0.521	0.545	4.40	1.04
B2	28.65	0.560	0.592	5.40	1.05
B3	29.32	0.602	0.642	6.23	1.06
B4	27.29	0.572	0.611	6.38	1.06
B5	26.99	0.591	0.632	6.48	1.06
B6	29.82	0.548	0.599	8.51	1.09
B7	26.36	0.572	0.632	9.49	1.10
B8	26.98	0.591	0.635	6.92	1.07

Table No.03 Evaluation data of Oxamniquine floating tablets

Formulation	**Thickness(mm) N=20**	**Weight variation n (mg)**	**Hard ness (kg/c m)**	**Friability (%)**	**Drug content (%)**	**Floating time (hrs.)**	**Floatinglag time (sec)**
B1	2.845±0.48	396.2±04	3.4±0.1	0.81%	97	12	42
B2	2.045±0.045	398.9±01	3.5±0.1	0.85%	90.35	14	50

B3	2.04±0.0	394.6±08	3.54.±0.3	0.84%	94.1	12	45
B4	2.73±0.02	395.7±06	3.59±0.3	0.79%	96.6	11	74
B5	2.385±0.5	394.1±01	3.69±0.3	0.81%	98.05	10	68
B6	2.41±0.04	404±07	3.89±0.3	0.86%	97.1	12	74
B7	2.345±0.3	399±06	3.99±0.3	0.81%	99.9	11.5	60
B8	2.14±0.14	398.504	3.98±0.2	0.83%	98.9	12	61

Table No.04 In vitro drug release formulationCumulative % drug release

Sr. No	Time	B1	B2	B3	B4	B5	B6	B7	B8
1	0	0	0.0	0	0	0	0	0	0
2	1	12.03	18.32	16.23	10.62	18.03	6.23	9.56	15.63
3	1.5	16.23	23.56	24.57	16.02	26.13	13.56	15.62	22.56
4	2	23.60	27.62	28.62	26.68	36.56	19.23	20.56	25.59
5	2.5	27.96	39.52	33.65	32.56	48.26	26.15	28.62	30.56
6	3	31.68	47.26	39.68	37.06	53.15	28.23	35.49	33.12
7	4	-	55.80	48.96	43.36	65.23	32.65	43.21	39.15
8	5	-	62.65	56.63	56.25	71.96	36.58	50.28	43.12
9	6	-	77.65	67.06	62.29	82.13	41.06	57.56	48.26
10	7	-	78.90	79.35	69.32	83.26	52.68	63.16	52.64
11	8	-	84.75	82.62	75.68	84.63	56.12	69.13	64.52
12	9	-	76.27	85.60	78.26	86.23	62.12	75.13	70.56
13	10	-	83.26	86.36	84.26	87.13	68.63	81.27	79.26
14	11	-	85.26	87.62	88.65	89.44	73.26	86.89	82.65
15	12	-	89.26	88.23	90.12	90.56	84.63	89.12	85.78
16	15	-	90.63	88.26	91.45	92.42	89.53	90.45	88.25
17	18	-	90.64	90.63	90.46	90.18	89.51	92.45	92.35
18	24	-	90.65	90.64	90.48	90.18	90.87	92.45	92.36

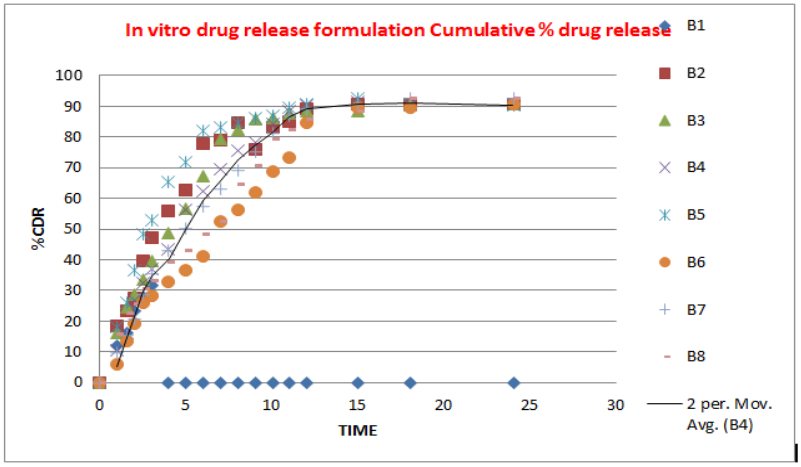


Fig No. 02 In vitro drug release formulation Cumulative % drug release

Table No. 05. % Swelling index

Sr. No	1hr	2hr	3hr	4hr	5hr	6hr	7hr	8hr
B1	25.44	35.74	42.32	50.32	60.65	75.58	80.98	90.30
B2	35.00	39.11	42.74	52.96	62.32	75.22	87.32	93.62
B3	42.22	51.32	62.32	75.74	84.38	87.36	102.32	106.35
B4	60.32	75.32	78.99	82.32	87.34	95.68	102.38	112.78
B5	65.32	75.33	82.36	85.85	88.87	98.54	105.87	121.32
B6	75.65	78.54	81.57	86.47	92.64	93.74	94.77	95.21
B7	79.32	81.21	82.47	88.54	93.45	96.57	104.32	109.65
B8	81.32	82.57	84.35	86.27	88.55	98.37	107.65	109.99

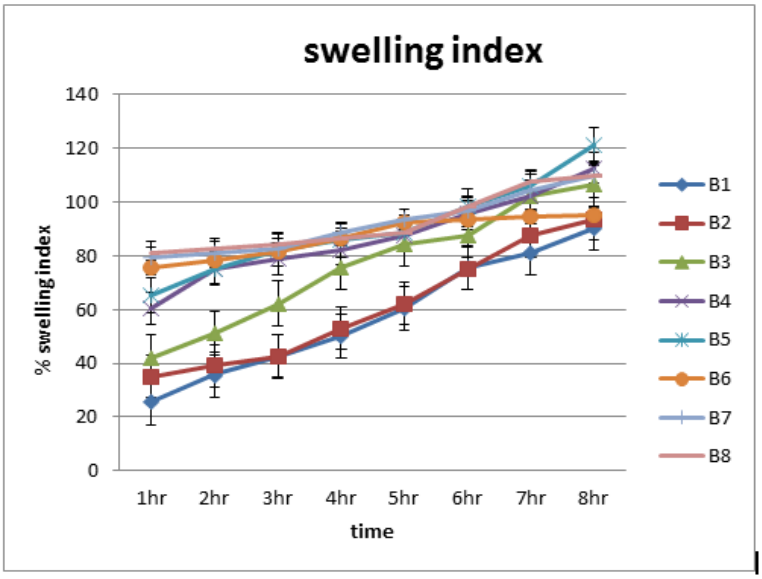


Fig No.03 % Swelling Index All Batches

Table No. 06 Data of stability studies of Oxamniquine tablet formulation at 40c/75%RH

TIME (DAYS)	B1 DC(mg)	B2 Dc(mg)	B3 Dc(mg)	B4 Dc(mg)	B5 Dc(mg)	B6 Dc(mg)	B7 Dc(mg)	B8 Dc(mg)
0	148.62	147.8	147.24	148.32	146.35	147.98	147.35	146.35
1	148.26	147.36	147.32	148.32	146.32	147.32	146.35	147.36
3	148.41	147.21	147.52	148.74	147.69	147.59	148.65	148.32
7	148.23	147.75	147.77	148.65	148.35	147.35	147.35	146.35
15	148.25	147.74	147.76	148.87	147.35	148.65	146.35	147.35
30	148.21	147.25	147.70	148.78	147.68	147.35	148.35	147.65
45	148.45	147.65	147.32	148.35	147.68	148.65	147.36	148.35
60	148.21	147.35	147.75	148.87	147.87	148.65	148.32	148.65
90	148.32	147.54	147.79	148.32	147.98	147.98	147.35	148.87

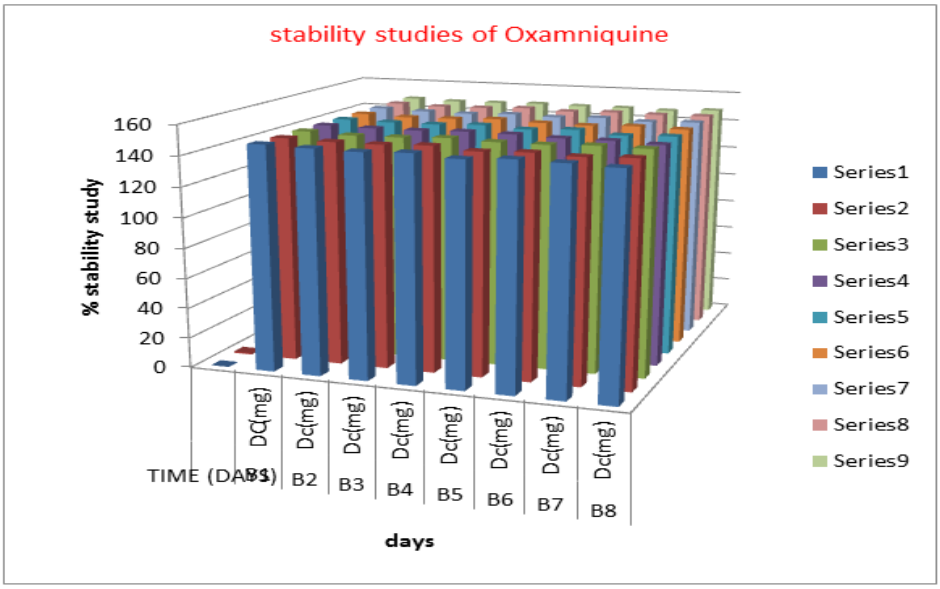


Fig No. 04 Stability studies of Oxamniquine All Batches Formulation

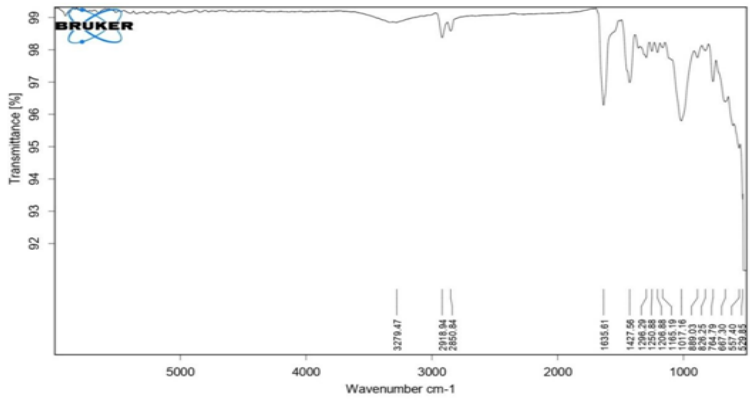


FIG NO.05 IR OF PURE DRUG OXAMNIQUINE

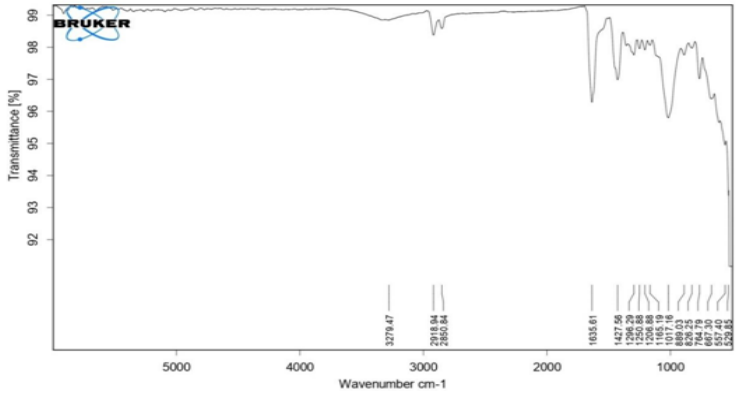
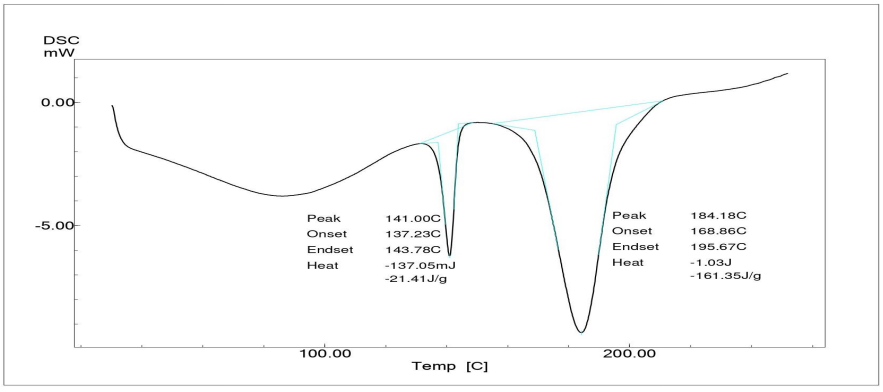


FIG NO.06 IR OF OXAMNIQUINE+TRAGACANTH+XANTHAN GUM



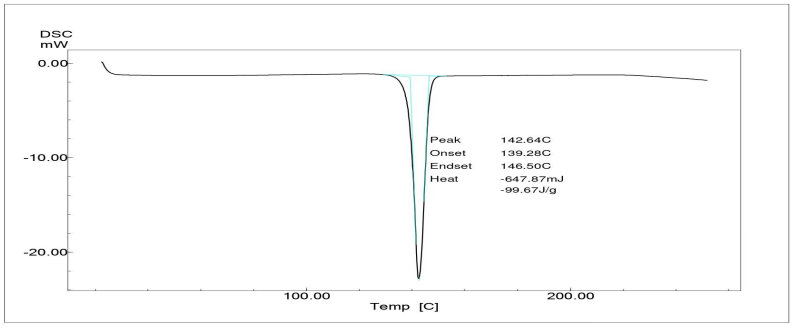
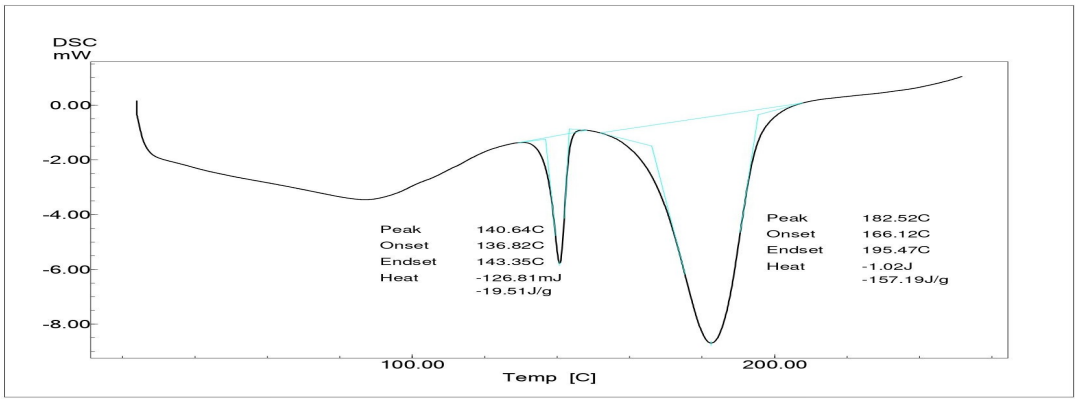


FIG NO.07 OXAMNIQUINE+XANTHAN GUM+GUAR GUM

FIG NO.08.PURE DRUG OXAMNIQUINE



FIGNO.09.DSC OF OXAMNIQUINE+TRAGACANTH+XANTHAN GUM

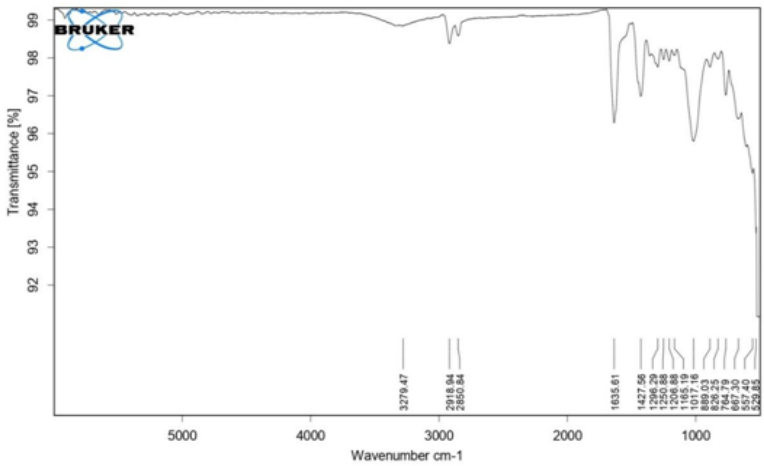


FIG NO.10 DSC OF OXAMNIQUINE+XANTHAN GUM+GUAR GUM

DISCUSSION:

The main aim of this work was to development new floating tablets Oxamniquine to increase its oral bioavailability by prolonging its gastric residence time and allowed to float in the stomach for a long period. In the present dissertation floating tablets of Oxamniquine were prepared by direct compression method using three polymers such as tragacanth, guar gum, xanthan gum Oxamniquine floating tablets were prepared by using tragacanth, guar gum, and xanthan gum (B1 to B6) and in B7 tragacanth and xanthan gum used. And in B8 xanthan gum, guar gum

used the powder evaluation suggested that all the prepared powders exhibited good flow properties, as the angle of repose value were less than 300 (table No.02) A good packing ability of the powder was indicated by car's index (table No.02). The weight, thickness and drug contents of all the tablets were found to be uniform. The hardness was in the range of 3.4 to 4.0 kg/cm2 and friability was in the range of 0.70 to 0.87% and drug content was in the range of 90 to 100 % ((Table No.03). The FT-IR study was carried out to find out the possible interaction between selected drug Oxamniquine and polymers as tragacanth, xanthan gum, guar gum. FT-IR of Oxamniquine showed the following peaks at 766.11, 1426.75, 1632.62, 2852.51, 2923.32, 2918.94, 1635.61, 1017.16, 1014.95, 1356.43, 1634.14, 2921.10 nm

B1 to B8 formulations were optimized based on floating time and drug release profile. The floating study of prepared tablets was carried out in 0.1N HCL buffer and the results shown in (table No.03). The differential scanning colorimetry (DSC) studies were performed on pure drug, and drug with polymers. The pure drug shows peak which is 150°c and the drug with polymers the peak at 175c, 150c, 155c, and 195c.were observed which indicates that there is no interaction between drug and polymers Refer Fig No. 08, 09 & 10 respectively. The in-vitro drug release study was performed using dissolution rate test apparatus in 0.1N HCL (pH 1.2), pH 7.4, and pH 9 the dissolution profiles are given in figure No 02. And the data presented in the tables No.04. From the dissolution data is evident that designed formulations have displayed in the range of 10% to 93 % drug release in 24 hrs. Among all the formulations, formulation B7 containing tragacanth and xanthan gum and B8 containing xanthan gum, guar gum. Shows % CDR 31 TO 92%. All the formulation was subjected for short term stability studies. It was observed for drug content at 40C for 90 days. There are no physical changes in appearance, flexibility and color. And B7 and B8 show good property.

CONCLUSION:

The goal of this study was to keep the dosage form in the stomach for a longer amount of time. This can be accomplished through the development of a floating drug delivery device. These tablets are primarily made to reduce lag time and may also improve bioavailability. Various polymers, such as tragacanth, guar gum, and xanthan gum, were used in the creation of floating tablets. Microcrystalline cellulose, pop k30, sodium bicarbonate, magnesium state (lubricant), and talc are among the other excipients employed. The lack of any drug/polymer/excipient interactions was established using Fourier transform infrared spectroscopy and DSC. The hardness, weight fluctuation, thickness, friability, drug content uniformity, buoyancy lag time, total floating time, swelling index, and in vitro dissolution tests of the manufactured floating tablets were all examined. B1, B2, B4, B5, B7, and B8 were the only eight formulas that exhibited good flotation. All of the formulations were tested for stability, and the B7 and B8 formulations were found to be stable. B7 & B8 reported maximum release of drugs to 92% within 24 hours. It was observed.

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