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Formulation and Evaluation of Sustained Release matrix tablets of Propranolol HCl with Gum Karaya

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Abstract : The main aim of the present work is to formulate and develop sustained release matrix tablets of Propranolol HCl. Selected method for preparation of sustained release matrix tablets of Propranolol HCl is wet granulation method by using varying concentrations of natural polymer, is Gum karaya as a release retardant. Total twelve formulations (PK1-PK12) were prepared by using different proportions of drug and Gum karaya (1:0.5, 1:1, 1:1.5, 1:2) with the aid of granulating fluids such as distilled water, ethanol and isopropyl alcohol. Excipients compatibility studies were carried out by FT-IR and DSC. All the matrix tablets of Propranolol HCl formulations were evaluated for pre-compression and post-compression parameters. All the formulations were evaluated for the hardness, friability, thickness, weight variation, drug content, and *in-vitro* drug release studies. Based on *in-vitro* drug release the polymer Gum karaya showed better dissolution control in all formulations, which is result of its release retardant characteristics. From 12 formulations PK4, PK8 and PK12 were optimized based on results from physicochemical evaluation and drug release studies. These formulations have composition of 1:2 ratio of drug and Gum karaya & they have shown more than 95% drug release at 12 hours. Hence based on studies, PK10 was selected for further studies by employing electrolytes (Sodium carbonate, Calcium carbonate, Magnesium carbonate) in different concentrations (25mg, 50mg and 75mg). These electrolytes were employed to examine matrix swelling and gel properties. The results indicated that the drug released at a controlled rate were due to differential swelling rate and matrix stiffening and provides a uniform gel layer. These findings indicated that the swelling and gel formation in the presence of ionisable species within the hydrophilic matrices provide an attractive alternative for controlled drug delivery from a monolithic system. The release kinetics of all formulations showed that the drug release followed fickian and non-fickian transport. The release kinetics of optimized formulation PKE8 showed fickian transport followed by zero order.

Keywords : Electrolyte, Propranolol, Gum karaya, matrix, sustained release.

Introduction

Sustained release dosage form is mainly designed for maintaining therapeutic blood or tissue levels of the drug for extended period of time with minimized local or systemic adverse effects. Sustained release dosage forms would be most applicable for drugs having short elimination half lives[1]. Propranolol hydrochloride, a nonselective beta-adrenergic blocking agent, has been widely used in the treatment of hypertension, angina pectoris, phaeochromocytoma, cardiac arrhythmias[2]and many other cardiovascular disorders. Propranolol hydrochloride undergoes extensive and highly variable hepatic first-pass metabolism following oral

administration, with a reported systemic bioavailability between 15% and 23%[3, 4].Propranolol hydrochloride has half-life of 3.9 $\pm$ 0.4 hours. So patients are routinely asked to take Propranolol hydrochloride for several times in a day. Such frequent drug administration may reduce patient's compliance and therapeutic efficacy. In recent years slow or sustained release formulations of Propranolol hydrochloride has become available with claims that these formulations maintain beta adrenoreceptor blockade throughout a 24 hours period and enable the drug to be given once daily. Propranolol hydrochloride has a short elimination half-life, which makes it a suitable candidate to be delivered at a controlled rate.Sustained release systems include any drug delivery system that achieves slow release of drug over an extended period of time. If the system is successful in maintaining constant drug levels in the blood or target tissue, it is considered as a controlled-release system.

The aim of the present investigation was to design and develop a novel oral monolithic, sustained release tablet dosage form of Propranolol hydrochloride with gum karaya as natural polymer along with pharmaceutically acceptable electrolytes which can induce in situ reactions between drug & electrolyte that alters drug release mechanism by matrix stiffening and changes in the gel would lead to extended drug release at a steady state manner has been elucidated.In the present work, a reliable process has been established for inducing in situ reactions between pharmaceutically acceptable electrolytes and drug which influences the intragel swelling dynamics and relative physical integrity of the swollen matrix structure. Furthermore, that may produce heterogenous domains with in the swollen gel boundary. In the past, alkaline compounds (or) buffers have been included in solid oral formulations for several acidic drugs that undergo dissolution rate limited absorption. The same principle of addition of buffers, osmotically active agents, surfactants (or) combinations thereof has also been utilized to control the swelling of hydrophilic polymers with different coating and inclusion techniques. However more specific strategy has been employed to apply the same principle to design a simple directly compressible, monolithic controlled release system. In general the application of buffers and ionizable compounds in dosage form design has essentially been limited to the minimization of localized GIT adverse effects and the solubility dependency of poorly soluble compounds. The aim of this work was to provide and expand on a means to design , formulate and develop a novel oral monolithic, controlled release tablet dosage form of a drug that may be tailored to provide quasi study state drug release over an extended period of time. The rationale behind the mechanism and dynamics of electrolytes induced matrix stiffening and structural changes to the gel is the basis of controlled drug release has also been elucidated[5-7].

Materials and Methods

Propranolol HCl was obtained as a gift sample from Pellets Pharma Limited, Hyderabad. Gum karaya purchased from Girijan co-operation society, Visakhapatnam. Avicel pH 102, Magnesium carbonate, Calcium carbonate, Sodium carbonate, Magnesium stearate, Talc and Isopropyl alcohol were procured from S.D Fine Chem. Ltd., Mumbai.

Preparation of Matrix Tablets

Propranolol HCl sustained release matrix tablets were prepared by wet granulation method[8-10] using drug: polymer ratios 1:0.5, 1:1, 1:1.5, 1:2. Weighed drug, gum karaya, avicel pH 102 (microcrystalline cellulose) & placed in motor then triturated well and then added distilled water, ethanol, isopropyl alcohol (granulating fluids) & prepared dough mass. Then dough mass was passed through sieve no. 14-16 for obtaining wet granules (wet screening). Then these wet granules were dried and they were passed through sieve no. 22 – 25 (dry screening). To dried granules added magnesium stearate & talc and mixed well. Tablets were prepared by using nine station tablet punching machine (Chamunda Pharmapvt Ltd, Ahmadabad), with use of punch size 8 mm for obtaining 350 mg of tablet weight.

Physical evaluation of tablets

Tablet hardness was determined with a Monsanto tablet hardness tester (Campbell Electronics, Mumbai, India). The individual hardness of 10 tablets randomly selected from each batch was measured and then mean and standard deviation taken. Whereas percentage friability of tablets was determined using a friabilator (Hoffmann-La Roche Ltd., Basel, Switzerland). The weight of ten tablets before and after the test, and the percent loss in weight recorded as friability [11,12]. The drug content of the tablets was evaluated spectrophotometrically (Shimadzu, model 1700) at 320 nm.

Swelling Index

The swelling behavior of a dosage form was measured by studying its weight gain. The swelling index of tablets was determined by placing the tablets in the basket of dissolution apparatus using dissolution medium at 37±0.5 ^{0}C. After 1, 2, 4, 6, 8 and 10 hours, each dissolution basket containing tablet was withdrawn and blotted with tissue paper to remove the excess medium and weighed on the analytical balance (Shimadzu, Ax120). The experiment was performed in triplicate for each time point. Swelling index was calculated by using the formula[13,14].

$$\text{Swelling Index} = \frac{\text{Wet weight of tablet - Dry weight of tablet}}{\text{Dry weight of tablet}}$$

In vitro drug release studies

In vitro drug release studies were carried out in pH 1.2 buffer solutions for 1 hour & pH 7.5 buffer solutions for 11 hours using USP apparatus 1 (Electrolab TDT-08L) at 50 rpm and 37 ± 0.5 °C. At predetermined interval, samples were withdrawn from the dissolution medium and replaced with fresh medium to maintain the volume constant[15,16]. After filtration and appropriate dilution, the amount of drug present in each sample was determined spectrophotometrically at 320 nm.

Dissolution Parameters

From the dissolution studies of various matrix tablets containing Propranolol HCl the following *in-vitro* kinetics like Zero Order-Release Rate Constant, First Order-Release Rate Constant, Higuchi's Diffusion Constant, and Korsermeyer-Peppas Constant were evaluated[17, 18].

Similarity factor

The similarity factor *f*2 as defined by FDA and EMEA is a logarithmic reciprocal square root transformation of one plus the mean squared (the average sum square) difference of drug percent dissolved between the test and reference products. It is given by following equation:

$$f_2 = 50 \times \text{Log}\{[\Sigma_{(n=1)}^{\infty} [Wt(Rt - Tt)^2]]^{-0.5} \times 100\}$$

An *f*2 value of 100 suggests that the test and reference profiles are identical and as the value becomes smaller, the dissimilarity between release profiles increases. The similarity factor (S_d) is given as

$$S_d = \sum_{t=1}^{n=1} \frac{\left[Log\left(\frac{AUCRRt}{AUCTt}\right)\right]}{n-1}$$

For the test and reference formulations to be identical, the $S_d$value should be zero.

Characterization of Matrix Tablets

Drug-excipients compatibility studies

FT-IR studies

By using dried KBr base line correction was taken. Weighed amount of the Propranolol HCl was carefully mixed separately along with KBr (dried at 40°-50°C) after that entire mixture was compressed using 10 ton pressure in a hydraulic press to produce a pellet after that it was subjected for scanning from 4000–400cm^{-1} using FT-IR 410 PC spectrophotometer. In the same way the method was adopted for polymers and formulations. The obtained spectrum from FT-IR was compared with drug and polymer mixtures.

DSC studies

The DSC thermal analysis of API, excipients and the mixtures of drug-polymers were studied in DSC analyzer model Universal V4.5A at a heating rate of 20^{0}C per min from 0 to 350^{0}C in a nitrogen environment.

DSC is a thermal analytical method performed to examine the drug and excipient compatibility. In this together test and standard were warmed from 20-300^{0}C and same temperature maintained during observation. Individually API and excipients includes polymers were scanned.

SEM studies

In scanning electron microscope as electrons are employed, a vacuum is maintained inside the microscope column to keep free of air molecules. Generally the column is maintained at a vacuum of about 10 torr. Now when a narrow beam of primary electrons are generated from the electron gun and hits the specimen surface then secondary electrons are emitted from the spot. The yield of the secondary electron depends on the angle between the direction of primary electrons and the specimen surface. A flat surface produces a minimum number of secondary electrons. If the beam is moved to another spot, there also the yields of secondary electrons would depend upon the topographical features of that region and maybe more or less than that of the first spot. Thus, continuous moving or scanning the electron beam over the specimen surface achieves a corresponding signal output. If the secondary electrons are also continuously collected and displayed on a cathode ray tube (CRT), an image appears which is comparable to the topographical detail of the specimen. The SEM study was carried out for matrix tablet to check the surface texture of the same. A smooth surface gives a uniform drug release whereas uneven or cracked surface gives an uncontrolled and non-uniform drug release.

Stability Studies

Stability studies on the optimized matrix tablets (PKE8) were carried out as per ICH guidelines at 25^{0}C ±20^{0}C/60% ± 5% RH and 40^{0}C ±2^{0}C/75% ± 5% RH for 6 months by storing the samples in stability chamber. Further, the matrix tablets were evaluated for appearance, weight variation, hardness, drug content and for in vitro drug release profiles over a period of 6 months.

Results & Discussion

The present work aimed to prepare and evaluate the sustained release matrix tablets of Propranolol hydrochloride for extended period of time. The tablets were prepared by using Gum karaya and pharmaceutically acceptable electrolytes by using wet granulation method. Compositions of various formulations are given in Table-1 & 2.

Table-1: Composition of Propranolol Hydrochloride Matrix Tablets.

	PK 1	**PK 2**	**PK 3**	**PK 4**	**PK 5**	**PK 6**	**PK 7**	**PK 8**	**PK 9**	**PK 10**	**PK 11**	**PK 12**
Propranolol HCl	80	80	80	80	80	80	80	80	80	80	80	80
Gum karaya	40	80	120	160	40	80	120	160	40	80	120	160
Avicel pH 102	223	183	143	103	223	183	143	103	223	183	143	103
Mg. stearate	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
Talc	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
Water	q.s	q.s	q.s	q.s	--	--	--	--	--	--	--	--
Ethanol	--	--	--	--	q.s	q.s	q.s	q.s	--	--	--	--
IPA	--	--	--	--	--	--	--	--	q.s	q.s	q.s	q.s
Total wt (mg)	350	350	350	350	350	350	350	350	350	350	350	350

Table-2: Composition of Propranolol hydrochloride matrix tablets with electrolytes.

Ingredients (mg)	PKE1	PKE 2	PKE 3	PKE 4	PKE 5	PKE 6	PKE 7	PKE 8	PKE 9
Propranol HCl	80	80	80	80	80	80	80	80	80
Gum karaya	80	80	80	80	80	80	80	80	80
Sodium carbonate	25	50	75	--	--	--	--	--	--
Calcium carbonate	--	--	--	25	50	75	--	--	--
Mg. carbonate	--	--	--	--	--	--	25	50	75
Avicel pH 102	158	133	108	158	133	108	158	133	108
Mg. stearate	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
Talc	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
IPA	qs	qs	qs	qs	qs	qs	qs	qs	q.s
Total Wt. (mg)	350	350	350	350	350	350	350	350	350

All prepared tablets with different electrolyte composition were within the weight range of 350 mg. Hardness of the matrix tablet formulations were constant for all batches maintained at 5 – 8 kg/cm^2. Friability loss for the formulations was negligible and was within the limits for all the batches. Drug content was uniform in all the batches of matrix tablet formulations. All the matrix tablets were prepared under identical conditions and were found to be stable. The results of physical parameters evaluated for various matrix tablets were given in Table 3.

Table-3: Physical evaluation parameters of Propranolol HCl matrix tablets with electrolytes.

Formulation code	Weight variation (%)	Friability (%)	Hardness (Kg/cm^2)	Drug content (mg)
PKE1	1.21±0.14	0.23±0.041	5.2±0.11	99.21±0.32
PKE2	1.27±0.15	0.42±0.016	5.4±0.22	98.70±0.24
PKE3	1.32±0.15	0.29±0.013	5.3±0.21	100.12±0.21
PKE4	1.25±0.21	0.95±0.043	5.4±0.21	99.76±0.23
PKE5	1.32±0.14	0.45±0.018	5.5±0.20	99.81±0.23
PKE6	1.05±0.04	0.23±0.012	5.5±0.26	98.69±0.17
PKE7	1.63±0.12	0.32±0.043	5.6±0.31	101.14±0.13
PKE8	1.15±0.14	0.47±0.044	6.0±0.20	99.17±0.23
PKE9	1.45±0.04	0.48±0.011	5.7±0.15	98.83±0.20

The physicochemical compatibility between drug and polymers was determined by FT-IR analysis. In spectra, additional peaks were observed due to polymers, apart from that, the spectra indicating no chemical interaction in Propranolol HCl and polymer mixtures. FT-IR spectrums of pure drug, combination of drugs with excipients and excipients spectra's were attained; the spectras were shown in Fig. 1 a and 1 b.

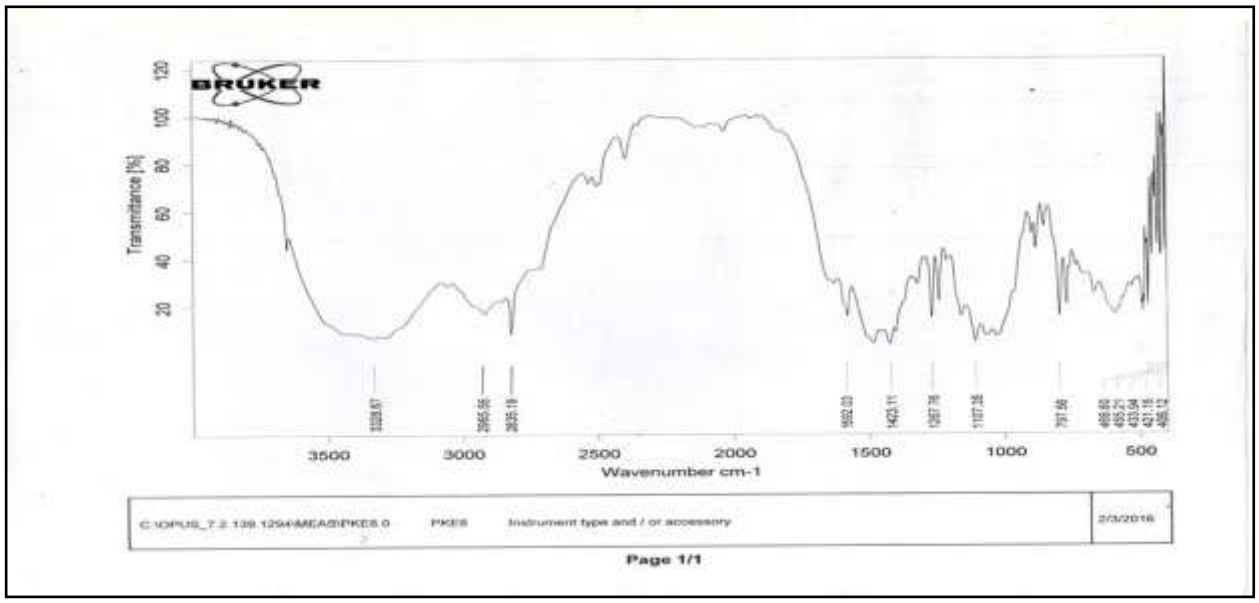

Fig. 1 a: FT-IR interpretation image of Propranolol hydrochloride Pure Drug.

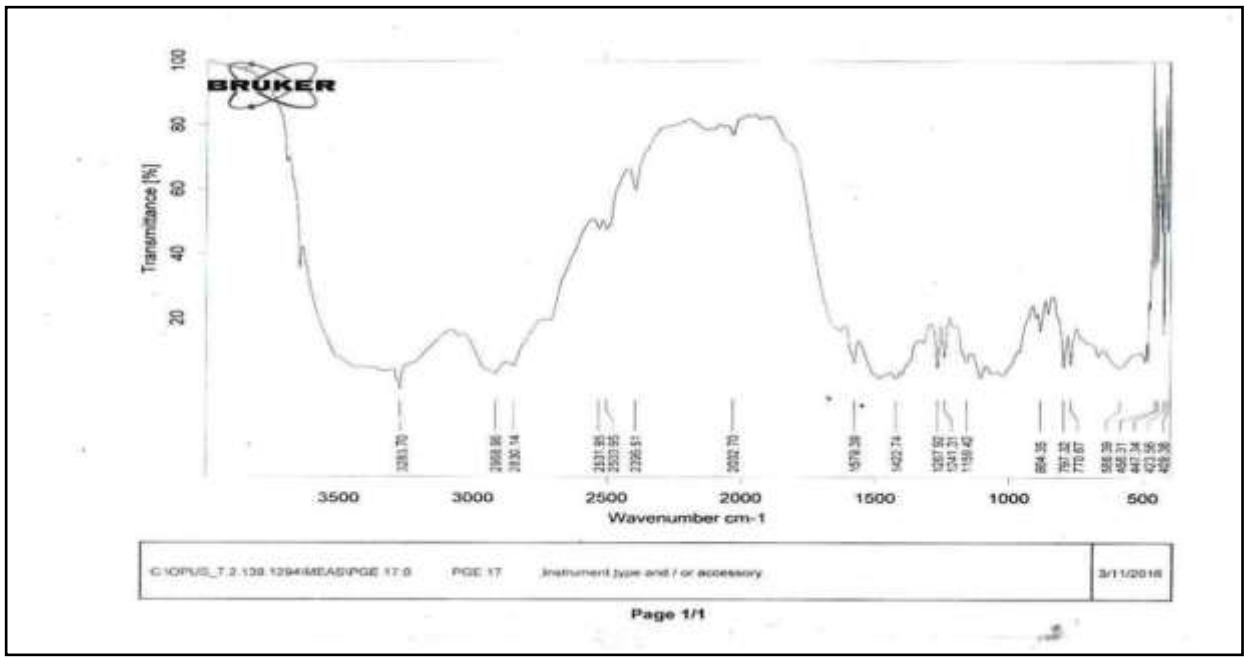

Fig. 1 b: FT-IR interpretation image of Propranolol hydrochloride optimized formulation PKE8.

In DSC analysis the Tg value of complexes (115.5^{0}C) were similar that of the Tg value of Propranolol HCl and confirming that there was no significant interaction between the drug and polymers. The DSC thermograms of pure drug and mixture of drug and polymers were shown in the Fig. 2& 3. In SEM images, it showed intact surface only swells without any perforations, channels, or troughs. After dissolution, the solvent front enters the matrix and moves slowly toward the center of the tablet. The drug diffuses out of the matrix after it comes in contact with dissolution medium. The images of the tablet showed a network in the swollen polymer through which the drug diffused to the surrounding medium. Thus, it was concluded that the drug was released from matrix by diffusion mechanism. During *in vitro* dissolution study, the polymer swells as the dissolution media enter into the polymer matrix. The surface becomes smooth and uniform which results in a slower and controlled drug release. SEM study of matrix tablets further confirmed both diffusion and erosion mechanisms. SEM images were shown in Fig. 4 & 5.

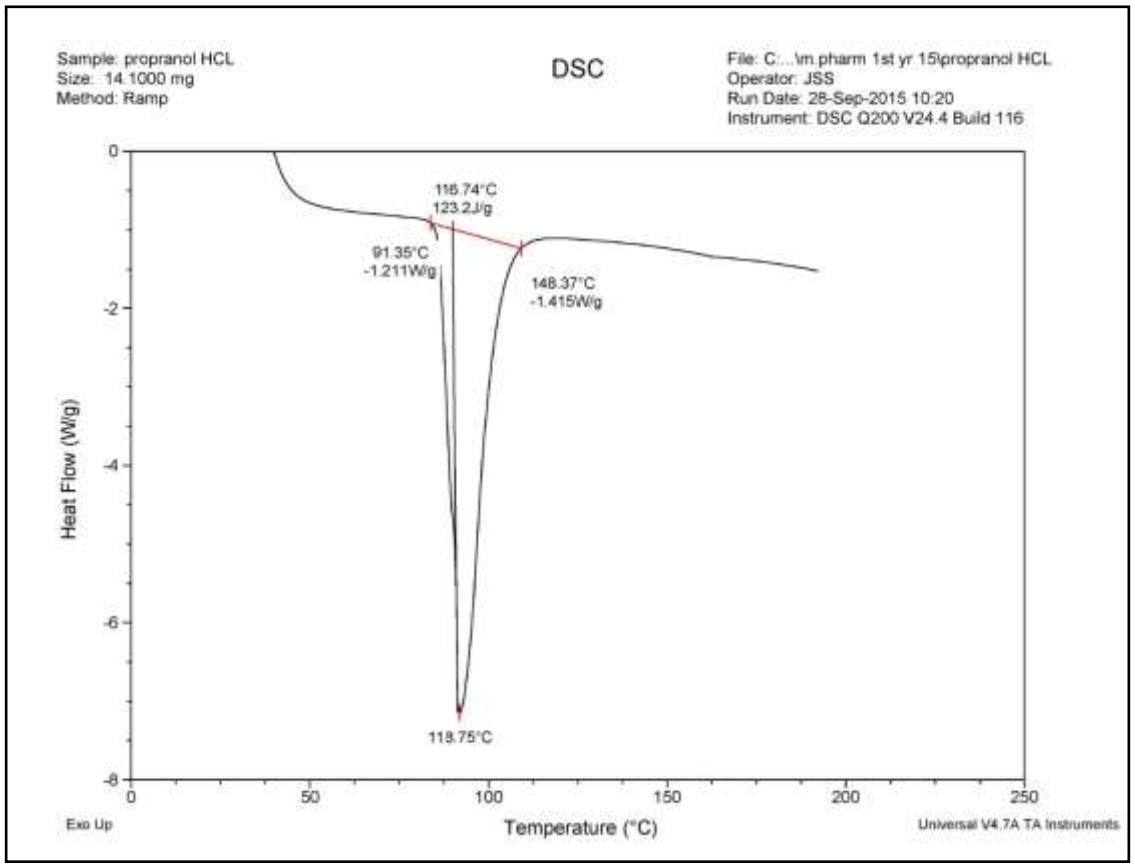

Fig. 2: DSC image of Propranolol hydrochloride.

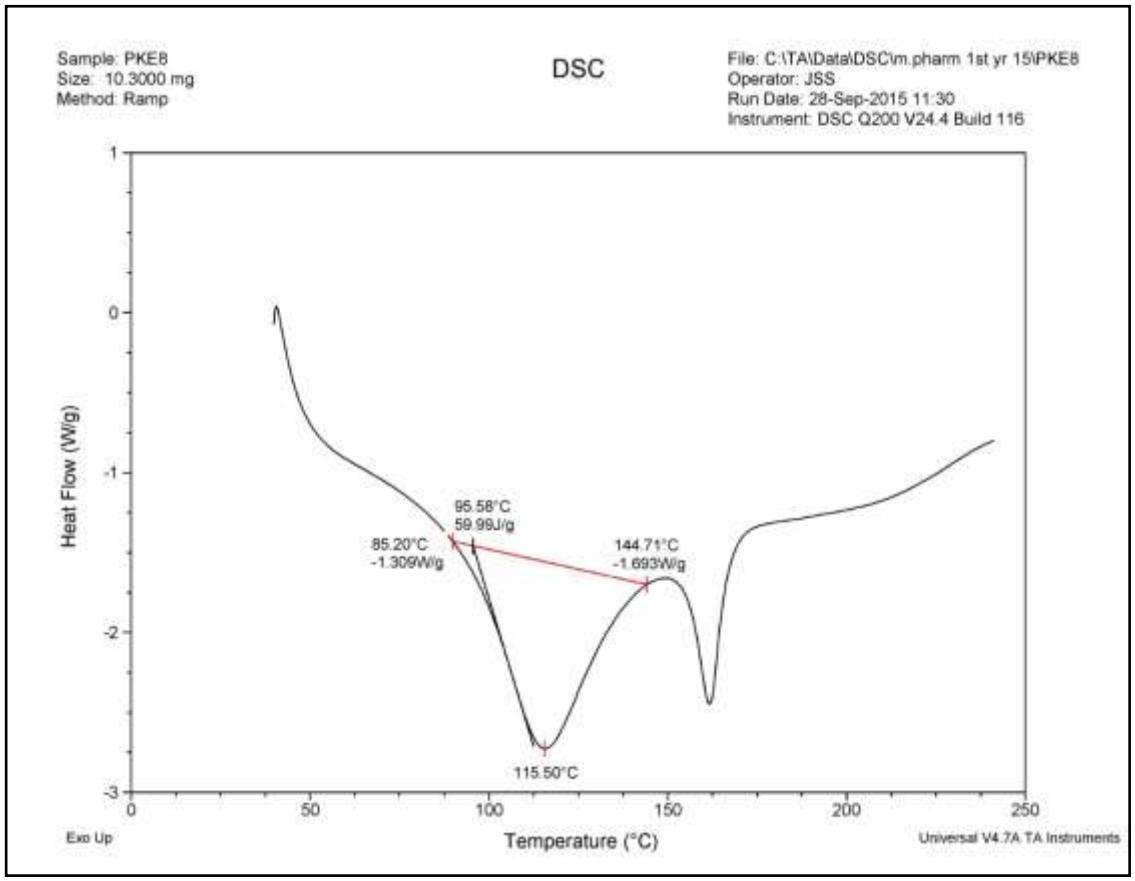

Fig. 3: DSC image of Propranolol hydrochloride optimized formulation PKE8.

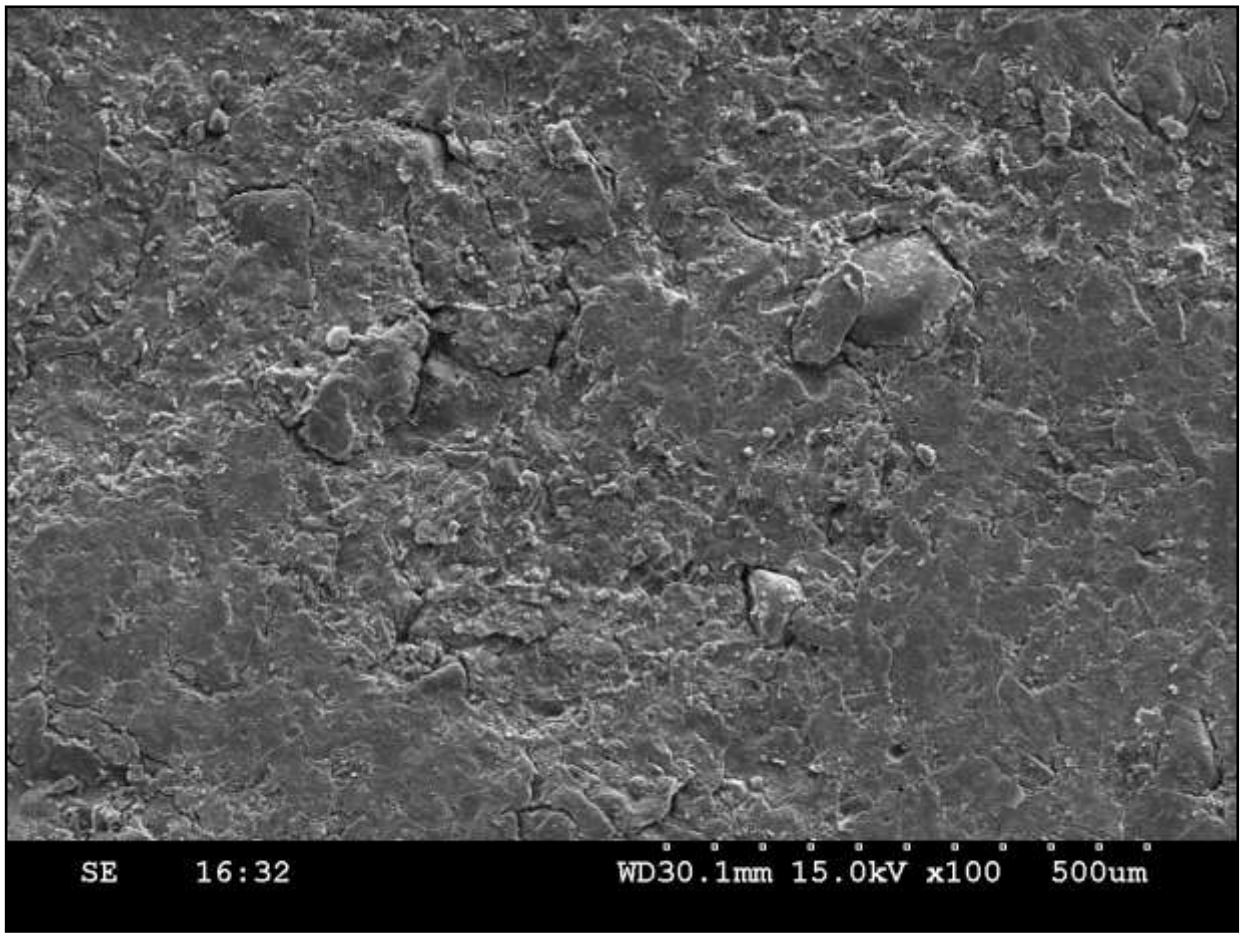

Fig. 4: SEM image of Propranolol hydrochloride optimized formulation PKE8 100X BMP before dissolution.

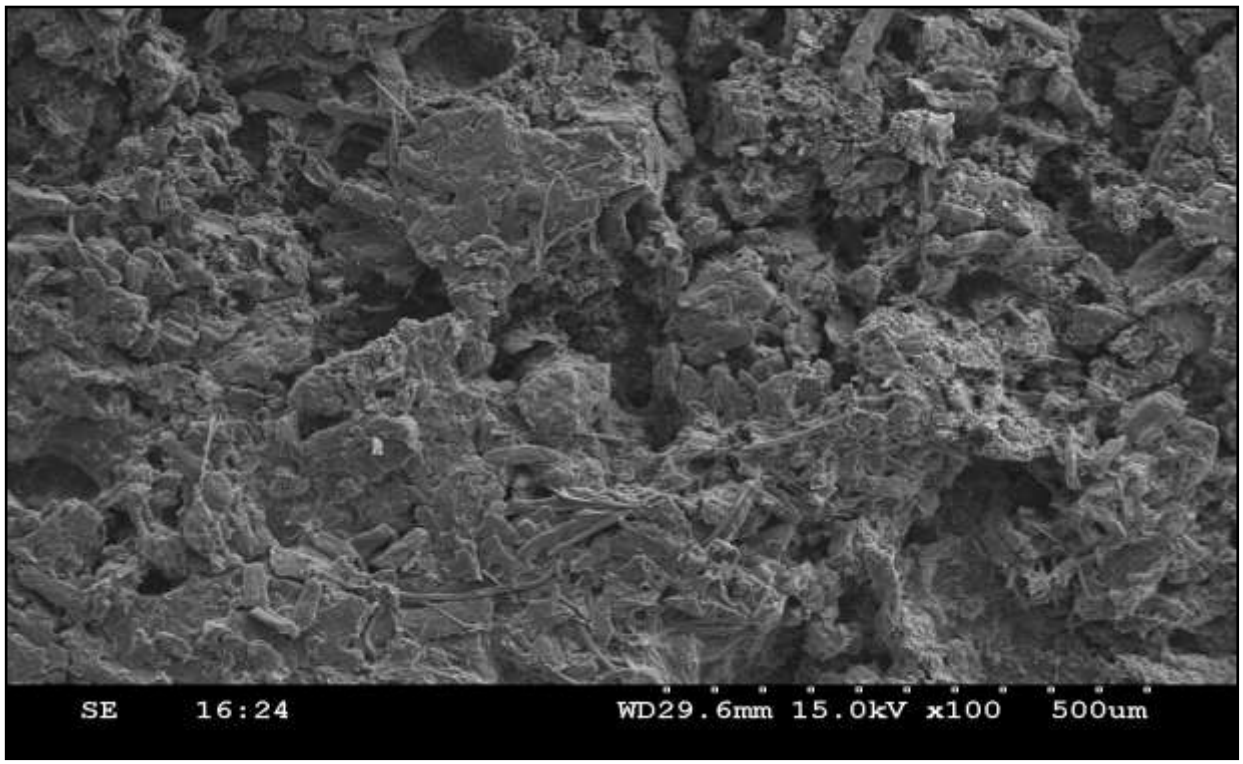

Fig. 5: SEM image of Propranolol hydrochloride optimized formulation 100X PKE8 BMP after dissolution.

The percentage of swelling in the formulations was very high during the dissolution. These matrix tablets were compressed without any electrolytes. The matrix tablet formulations having electrolytes were exhibited low swelling rate during the first 2-6 hrs followed by gradual increase in the swelling. Difference in swelling of the tested hydrophilic polymers could be explained by the difference in resistance of the matrix network structure to the movement of dissolution medium. In addition, the presence of a water-soluble drug might have improved the surface wetting of the matrix. Initial swelling percentage was little low in all formulations and later the rate of swelling was gradually increased due to competition in uptake of media by the drug and electrolytes. The swelling index values for formulations were given in Table 4 & 5.

Table-4: Swelling characteristics of selected matrix tablet formulations.

Time (hrs)	**Percentage Swelling Index**		
	PK4	PK8	PK12
1	64.89	59.96	60.67
2	85.94	80.77	79.96
4	115.67	113.46	112.46
6	133.67	128.47	127.78
8	157.89	156.64	157.79
10	165.39	162.49	161.64

Table-5: Swelling Index of selected Propranolol HCl matrix tablets with electrolytes.

Time (hrs)	**Percentage Swelling Index**		
	PKE2	PKE5	PKE8
1	54.69	54.21	56.98
2	75.69	74.98	77.89
4	105.46	106.49	109.29
6	121.98	122.29	125.79
8	144.39	145.67	147.86
10	155.79	155.89	158.82

The percentage drug content for different tablets formulations were varied from 98.69% to 101.14% indicating the uniformity in drug content. Polymer dissolution controlled drug release systems are made of a drug molecularly dispersed or dissolved in a polymeric matrix. As medium penetrates the polymer, swelling occurs and a thin layer of polymer in the rubbery state (gel layer) is formed. Drug diffusion through this gel layer is relatively fast. During this diffusion process, as swelling and dissolution are competing, at the beginning the gel layer thickness increases due to swelling, and then remains constant due to synchronization of swelling, resulting in drug diffusion, dissolution, and finally as dissolution take over. During the dissolution process, the polymer carrier passes through three distinct regimes of macromolecular configuration. It was also observed that increase in the concentration of gum, the drug release was extended. This is due the hydrophilic nature of the gum. These tablets showed greater medium uptake which resulted in the formation of highly viscous gel layer around the tablet [13,14]. The formed gel layer resulted in the longer diffusional path length, there by retarding the drug diffusion. The critical value of ‘n’ calculated for these formulations indicated non-fickian diffusion i.e., the drug release is by diffusion from the hydrated matrix and by polymer erosion.The inclusion of electrolytes within a swollen matrix for controlling the release rate of drug may lead to the formation of free base of Propranolol HCl and fundamental structural changes in gel boundary, thus inducing the textural variations in the swollen matrix. It appears that electrolyte induced buffer threshold within the matrix place an essential role in effective interaction with drug and textural changes. An inverse relationship was observed between concentration of polymer and release rate of drug from the matrix tablets [15]. Upon model fitting analysis of matrix tablets, it was found that the release of drug from matrix tablet follow zero order kinetics with anomalous diffusion. Peppa’s model with ‘n’ values and the correlation coefficient ‘r’ values were shown in Table 6.

Table-6: Release kinetics of various matrix tablets with electrolytes formulations.

Formulation code	Zero order K	R^2	First order $K(hr^{-1})$	R^2	Higuchi's $K(m.g.h^{1/2})$	R^2	Koresmayer & Peppas N	R^2
PKE1	3.12	0.821	0.231	0.933	11.31	0.941	0.421	0.947
PKE2	4.21	0.740	0.137	0.934	12.62	0.977	0.562	0.966
PKE3	4.30	0.977	0.230	0.960	14.33	0.932	0.423	0.973
PKE4	4.14	0.821	0.171	0.934	12.75	0.973	0.533	0.962
PKE5	5.31	0.932	0.136	0.978	9.78	0.934	0.462	0.927
PKE6	5.21	0.877	0.215	0.944	10.10	0.977	0.551	0.965
PKE7	5.86	0.7245	0.144	0.934	8.12	0.925	0.414	0.931
PKE8	5.32	0.987	0.264	0.983	9.94	0.972	0.536	0.914
PKE9	4.71	0.843	0.130	0.845	14.70	0.911	0.545	0.942

As the proportion of the polymer was increased, the release of drug was decreased to certain extent. Good linear relationship was observed between polymer concentration and drug release to certain extent. The electrolyte employed has significant influence on drug release from the matrix tablet composed of natural polymer. The electrolytes employed in the study are calcium carbonate, magnesium carbonate and sodium carbonate. The rate of release from these matrix tablets prepared with different electrolytes in each case was found to be first order and controlled by both diffusion and dissolution mechanisms. The influence of each and individual electrolyte on drug release were given below;

Electrolytes have high influence on drug release from the matrix tablets of drug. The drug release was slow and extended for prolonged period as the concentration of electrolyte was increased. Electrolytes at higher concentration (75mg/tablet) exhibited greater inhibition in drug release from matrix & at lower concentration (50mg/tablet) showed controlled release of the drug. The concentration of electrolyte at 50 mg per tablet concentration was found to produce ideal drug release from the matrix tablets. The influence of retardation of drug release by various electrolytes was in the order of;Sodium carbonate > Calcium carbonate > Magnesium carbonate.

The drug release profile from the developed formulations manufactured in this study was compared to the marketed product. It was found that the *in-vitro* dissolution profile of drug from test product containing natural polymer is almost similar with that of the marketed product. The results of this study indicated that the release of drug from the marketed as well as test product followed Zero order of release kinetics via anomalous (non-fickian) diffusion.

The similarity and the dissimilarity factors depict that the drug release from the prepared batches were significantly different from the release of drug from the marketed tablet. The significance of using similarity factor was to compare the solubility and release profile of the prepared tablets with that of the marketed tablets. The f2 value was found to vary from 11 to 64. The f1 value ranged from 9 to 103. Table 8 represents the similarity and the dissimilarity factors for the various batches.

Table-7: Similarity factor for optimized matrix tablet with electrolyte formulation (PKE8) in comparison with marketed formulation.

Similarity factor f2	64
Difference factor f1	9

The similarity and the dissimilarity factors indicate that the sustained release formulations are quite different from the marketed tablet, and more sustained than the marketed tablet. It may thus be concluded that the sustained release formulation can be achieved using hydrophilic polymers, which can also maintain the sustained release profile over an extended period of time.

The stability studies on the optimized matrix tablets (PKE8)were carried out for 6 months as per ICH guidelines. Under the specific storage conditions, no significant changes in the physicochemical properties viz., weight of the tablet, hardness, friability and drug content of matrix tablets was observed. The result of stability tests suggested that drug release properties from the prepared tablets were stable under the above storage conditions and no significant changes in their physical attribute was observed.

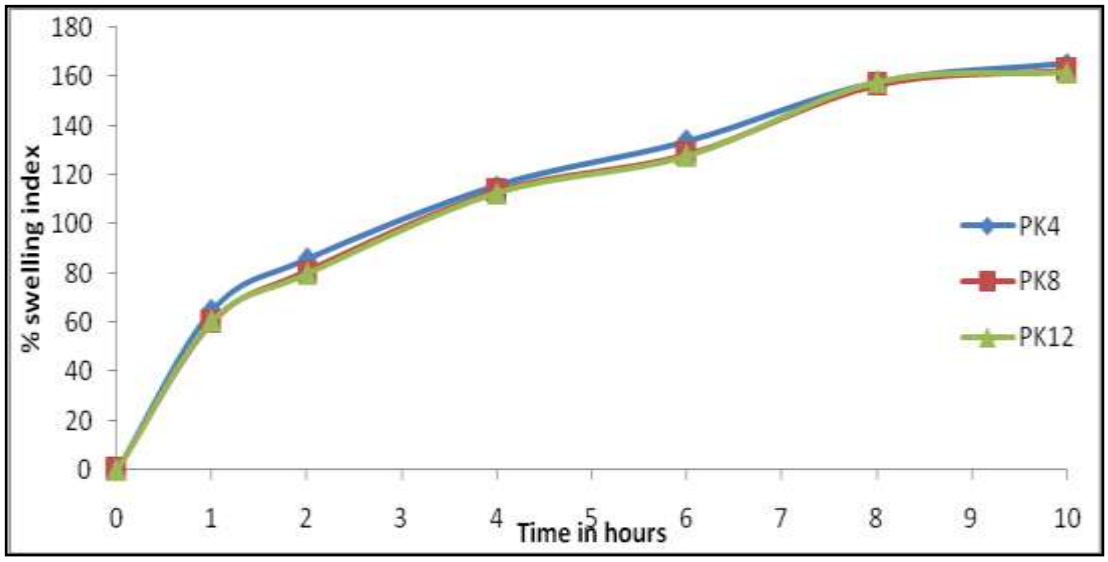

Fig. 6: Percentage swelling profiles of sustained release formulations of Propranolol hydrochloride.

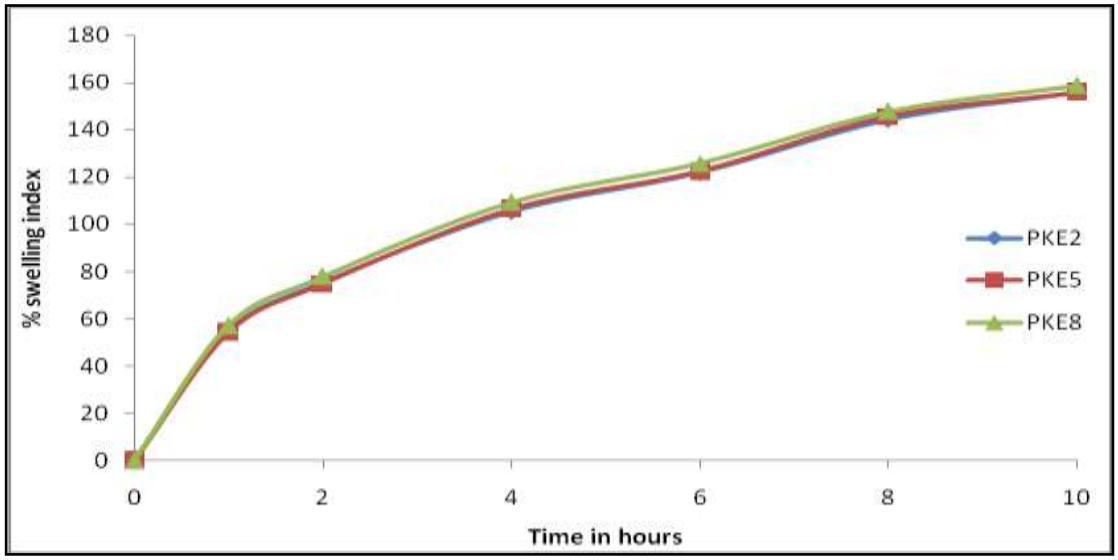

Fig. 7: Percentage swelling profiles of sustained release formulations of Propranolol hydrochloride with electrolytes.

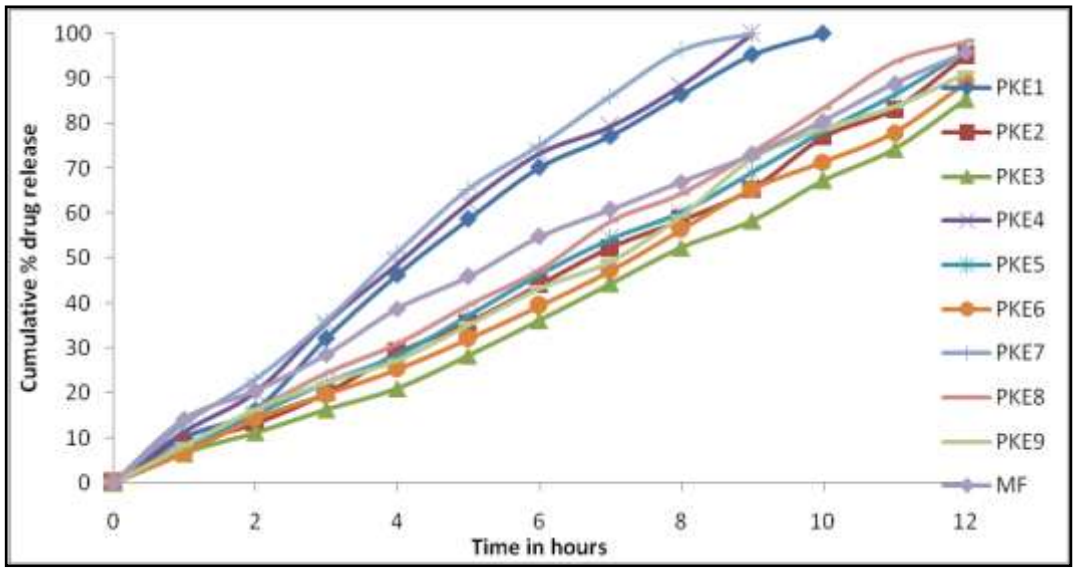

Fig. 8: Drug release profiles of various sustained release formulations of Propranolol hydrochloride with electrolytes in comparison with marketed formulation.

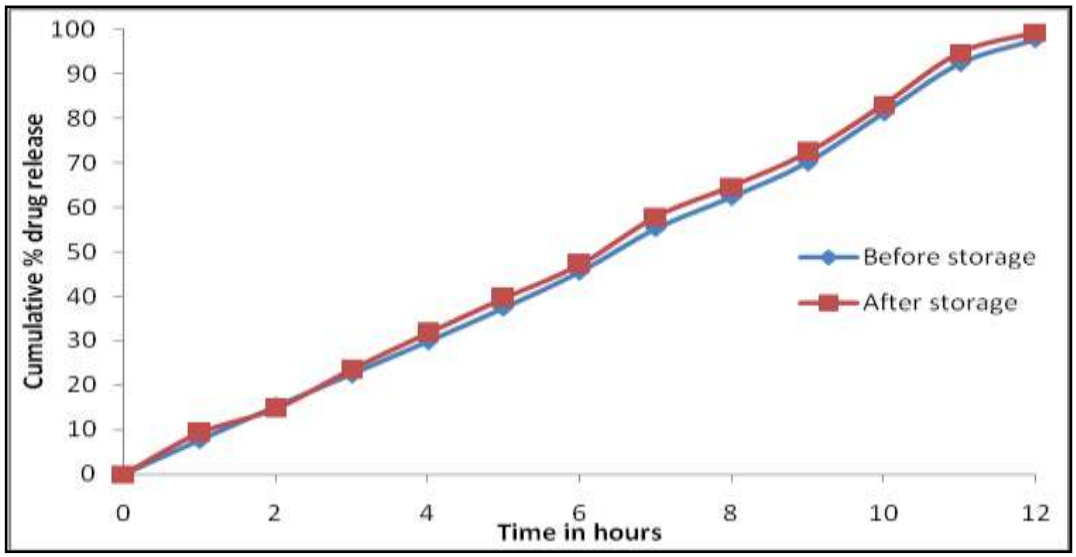

Fig. 9: Stability profile of optimized formulation (PKE8) before and after storage.

Conclusion

Propranolol HCl sustained release matrix tablets were successfully formulated using the combinations of natural gum such as gum karaya with electrolytes for delivery of drug over an extended period of time. Previous studies have shown that natural gums like xanthan gum, guar gum, karaya gum and sodium alginate alone in the tablets cannot efficiently control the drug release for prolonged period of time. This study demonstrates that the combination of hydrophilic natural gum and electrolytes with optimum concentrations led to prolonged release of the drug up to 12 hrs. An important feature of this system is the potential for generating constant drug release.

The physical parameters were satisfactory and obtained within IP specified limits. The FT-IR studies revealed the absence of drug-polymer interaction. The optimized formulation PKE8 was able to control the drug release up to 12 hours. The formulated sustained release tablets can decrease, the frequency of drug administration and it can decrease the plasma drug fluctuation and it can improve the patient compliance. In this study it was also found that the concentration of polymer have also a tremendous effect on drug release rates, by increasing the amount of polymer, drug release rate can be reduced to a high value. The tablets showed good stability and physicochemical characteristics.

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