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PROPRANOLOL HYDROCHLORIDE LOADED NANOSPHERES: DEVELOPMENT AND CHARACTERIZATION

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ABSTRACT: Nanotechnology is widely used for delivery of various drugs to the body for increasing the bioavailability, reducing toxicity and controlled release. Nanospheres are the solid particles which are spherical in shape, having the particle size range between 1-1000 nm and having better bioavailability. In nanospheres, the drug is physically and uniformly dispersed in the matrix system of the polymer. Nanospheres of Propranolol Hydrochloride were prepared by using solvent evaporation technique with different concentration of Eudragit RS100 and Eudragit RL100 polymers. The different formulation factors like drug: polymer ratio, concentration of solvent, stirring speed, stirring time on particle size, drug encapsulation, drug efficiency, surface morphology, and process yield and drug release behavior was studied. The *in-vitro* performance of nanospheres were evaluated by recovery efficiency, particle size analysis, surface topography (using scanning electron microscopy), drug-polymer compatibility (using differential scanning calorimetry) and drug release studies. The single emulsion solvent evaporation method used for nanospheres preparation was suitable in the particle size range between 265.67±3.98 nm, the encapsulation efficiency was 74.67±2.56% (w/w) and the process yield was 83.23±1.23% (w/w). Scanning Electron Microscope (SEM) showed that nanospheres were having spherical in shape. FTIR showed no potential chemical interaction between the drug and polymer used. *In vitro* release studies revealed that drug release from nanospheres followed Higuchi kinetics.

INTRODUCTION: Propranolol hydrochloride is a sympatholytic non-selective beta blocker. Scottish scientist James W. Black successfully developed propranolol in the 1960. In 1988, he was awarded with the Nobel Prize in medicine for this discovery.

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Propranolol was derived from the early β-adrenergic antagonists dichloroisoprenaline and pronethalol. It is used in the treatment of essential hypertension, myocardial infarction and arrhythmia. Propranolol hydrochloride is completely absorbed from the G.I. Tract following oral Administration. It undergoes extensive hepatic first pass metabolism.

Propranolol hydrochloride is about 90% bound to plasma protein; bioavailability is 26% and biological half-life ($t_{1/2}$): 4-5 hr.

Propranolol hydrochloride is metabolized in the liver and the main metabolites are naphtoxyl acetic acid (42%), 4-hydroxypropranolol (41%) and Propranolol-O-glucuronide (17%). Efficacy of the administered dose may get diminished due to the incomplete drug release from the device above the absorption zone. Propranolol hydrochloride requires multiple daily drug dosage in order to maintain adequate plasma concentration. Because of this and rather high frequency of administration, it is necessary to develop sustained release preparation with extended clinical effect [1, 2].

MATERIALS AND METHODS:

Materials: Propranolol hydrochloride was supplied as a gift by Ranbaxy Laboratories Limited, Baddi, India. Eudragit RS 100 and Eudragit RL 100 were supplied by Evonik Industries AG, Mumbai, India. Magnesium Stearate was supplied by Loba Chemical Private Limited, Mumbai and n-hexane, Liquid Paraffin heavy, acetone, methanol were obtained from from Merck Specialties Private Limited, Mumbai. All other chemical reagents were of analytical grade and were used without any further purification.

Methods:

Preparation of Nanospheres: In this method, Drug-Propranolol HCl and polymers (Eudragit RS 100 & Eudragit RL 100) in 1:3 ratio were dissolved in 10ml water miscible organic solvent (Acetone & Methanol 2:1) as internal phase in 100 ml beaker (beaker 1). Then this mixture was kept on a magnetic stirrer till it appeared as a clear solution with the aid of magnetic bead with approximately 10 minutes of stirring at 400-500 rpm. Liquid paraffin (100 ml) as external phase containing n-hexane (7.5 ml) was taken in a 500 ml beaker and was stirred with the help of magnetic stirrer (beaker 2).

The drug polymer mixture of beaker 1 (internal phase) was added drop wise to beaker 2 (external phase) and stirred with a magnetic stirrer (REMI, Mumbai, India) at a stirring speed of 1200 rpm. After 4 hrs of continuous stirring, until solvent was evaporated, nanospheres were isolated by centrifugation (REMI, Mumbai, India) at 19000 rpm for 20 mins and washed with petroleum ether to remove the impurities with the aid of 0.2 μm filter paper and dried overnight at room temperature [3].

In the study the effect of the following formulation variable on the nanosphere size, surface morphology, drug loading and encapsulation efficiency were investigated [4, 5].

1. Polymer: drug ratio: This was investigated by variation in the polymer: drug ratio (1:1, 2:1, 3:1, 4:1 and 5:1, w/w).
2. n- hexane concentration: (5%, 7.5%, 10% v/v)
3. Aqueous : Oil phase ratio: (1:5, 1:10, 1:15)
4. Stirring speed: (400, 800, 1200, 1600)
5. Stirring time: (1, 2, 3, 4 hr)

RESULT AND DISCUSSION: The solvent evaporation/extraction techniques are commonly used for the nanoparticles preparation to extend the release of drugs. These techniques can be utilized for the encapsulation of either water insoluble or water soluble drug with hydrophobic polymers.

In this study, the single emulsion solvent evaporation method has been selected to entrap water soluble drug in nanospheres. In this method, Drug-Propranolol HCl and polymers (Eudragit RS 100 & Eudragit RL 100) in 1:3 ratio were dissolved in 10ml water miscible organic solvent (Acetone & Methanol 2:1) as internal phase in 100 ml beaker (beaker 1). Then this mixture was kept on a magnetic stirrer till it appeared as a clear solution with the aid of magnetic bead with approximately 10 minutes of stirring at 400-500 rpm. Liquid paraffin (100 ml) as external phase containing n-hexane (7.5 ml) was taken in a 500 ml beaker and was stirred with the help of magnetic stirrer (beaker 2).

The drug polymer mixture of beaker 1 (internal phase) was added drop wise to beaker 2 (external phase) and stirred with a magnetic stirrer (REMI, Mumbai, India) at a stirring speed of 1200 rpm. After 4 hrs of continuous stirring, until solvent was evaporated, nanospheres were isolated by centrifugation (REMI, Mumbai, India) at 19000 rpm for 20 mins and washed with petroleum ether to remove the impurities with the aid of 0.2 μm filter paper and dried overnight at room temperature and solidifies nanospheres obtained [6, 7, 8].

Polymer: drug ratio: Propranolol hydrochloride loaded nanospheres were prepared using different polymer: drug ratio (from 1:1, 2:1, 3:1, 4:1, 5:1, w/w) by variation in the weight of polymer dissolved in acetone and methanol to investigate the eventual modification of the particle size, drug loading, efficiency of entrapment and process yield. Increasing the weight of polymer in a fixed volume of organic solvent resulted in decrease in mean particle size (from 730±2.53 nm to 220±1.06 nm for 1:1 to 3:1).

Further increasing the weight of polymer in fixed volume of solvent resulted in increase in mean of particle size (from 470 ± 1.12 nm to 900 ± 2.07 nm for 4:1 to 5:1). This is in agreement with the finding of Jeffery et al. (1991), suggesting that the higher weight of polymer in the sample may have led to an increased frequency of collision, resulting in fusion of semi-formed particles and finally producing an overall increase in the size of the nanospheres [9].

Moreover, the higher weight of polymer in the emulsion droplets may have led to an enhancement of the efficiency of the drug entrapment because the high viscosity of the organic phase tends to restrict migration of the inner aqueous/drug phase to the external water phase up to certain polymer weight limit, further increase in polymer weight decrease the encapsulation efficiency. Whereas, for 1:1 polymer: drug ratio the particles obtained were spherical in shape but with a rough surface and a mean diameter of 730 ± 2.53 nm, a process yield of 58.05±1.06% (w/w), an encapsulation efficiency of 42.46±2.52% (w/w) and a drug loading of 21.54±1.23 % (w/w).

Further increase in polymer: drug ratio from 2:1 to 4:1 led to the mean diameters of 550±1.92 nm, 220±1.06 nm and 470±1.12 nm, the process yields of 66.26±2.12% (w/w), 81.42±1.44% (w/w) and 64.16± 1.78% (w/w), the encapsulation efficiencies of 56.16±1.88% (w/w), 70.42±1.67% (w/w) and 64.86± 2.52% (w/w) and the drug loadings of 19.72±1.09% (w/w), 17.68±2.13% (w/) and 13.88 ± 1.07% (w/w), respectively.

A further increase in polymer: drug ratio, i.e., 5:1 led to production of spherical particles in aggregates with a mean diameter of 900±2.07 nm, a process yield of 62.28±1.02% (w/w), an encapsulation efficiency of 61.96±1.09% (w/w) and a drug loading of 12.36±2.12% (w/w) [10, 11, 12].

TABLE 1: EFFECT OF POLYMER: DRUG RATIO ON NANOSPHERES CHARACTERISTICS

Batch code	Polyer: Drug Ratio (w/w)	Mean diameter[a] (nm)± s.d.	Drug loading[a] (%,w/w) ± s.d.	Entrapment efficiency[a,c] (%, w/w) ±s.d.	Process yield[a,b] (%w/w) ± s.d.
PE-1	1:1	730 ± 2.53	21.52 ± 1.23	42.46 ± 2.52	58.05 ± 1.06
PE -2	2:1	550 ± 1.92	19.72 ± 1.09	56.16 ± 1.88	66.26 ± 2.12
PE -3	3:1	220 ± 1.06	17.68 ± 2.13	70.42 ± 1.67	81.42 ± 1.44
PE -4	4:1	470 ± 1.12	13.88 ± 1.07	64.86 ± 2.52	64.16 ± 1.78
PE -5	5:1	900 ± 2.07	12.36 ± 2.12	61.96 ± 1.09	62.28 ± 1.02

[a] Data represent the mean of three independent experiments. [b] Percentage of weight of nanospheres recovered with respect to weight of polymer utilized. [c] Percentage of encapsulated drug with respect to the total amount use.

Concentration of n-hexane in the External Aqueous Phase: Concentration of n-hexane is an important parameter because it is responsible for hardening and stability of nanospheres in dispersion phase. Various concentrations of n-hexane (5, 7.5, 10 % v/v) were studied.

Amongst the 7.5 % v/v concentration of n-hexane resulted in successful preparation of nanospheres. With 7.5 % v/v n-hexane concentration showed mean diameters of 305.02±2.09, processing yield 79.45±2.78 and encapsulation efficiency 79.45±2.78. With 5 % and 10 % v/v concentration of n-hexane showed mean diameters respectively 700.56±1.54, 450.98±3.09, processes yield 64.76±1.89, 67.65±2.4 and encapsulation efficiency 65.09±2.34 and 68.98± 2.87.

For all the n-hexane concentration in our experimental conditions, respective emulsion droplets formed during the agitation seemed to be stable enough to harden after solvent evaporation and form the nanospheres [13].

TABLE 2: EFFECT OF CONCENTRATION OF N-HEXANE IN THE EXTERNAL AQUEOUS PHASE

Batch code	n-hexane conc. (% v/v)	Mean diameter[a] NM ± s.d.	Drug loading[a] (%,w/w) ± s.d.	Entrapment efficiency[a,c] (%,w/w) ± s.d.	Process yield[a,b] (%w/w) ± s.d.
HPE- 1	5	700.56 ± 1.54	16.80 ± 1.67	65.09 ± 2.34	64.76 ± 1.89
HPE- 2	7.5	305.02 ± 2.09	18.65 ± 2.65	71.09 ± 1.87	79.45 ± 2.78
HPE- 3	10	450.98 ± 3.09	15.09 ± 5.09	68.98 ± 2.87	67.65 ± 2.4

[a] Data represent the mean of three independent experiments. [b] Percentage of weight of nanospheres recovered with respect to weight of polymer utilized. [c] Percentage of encapsulated drug with respect to the total amount use.

Aqueous: Oil Phase Ratio: As external dispersing phase different volumes of Liquid paraffin oily solution (50, 100, 150 ml) were employed, resulting in different ratios between oily external and aqueous internal phases (w/o ratio), namely 1:5, 1:10, 1:15. Table 4.5, summarizes the obtained results. The polymer: drug ratio was 3:1. The use of the lower w/o ratio (1:5, i.e., 50 ml) led to formation of irregular nanospheres with a mean diameter of 700.34±0.56 nm, a process yield of 62.45±2.98% (w/w), an encapsulation efficiency of 65.87±2.98% (w/w) and drug loading of 16.45±2.78% (w/w). The highest o/w ratio (1:15, i.e., 150 ml) led to an aggregates of particles after isolation. Conversely particles produced by a 1:10 o/w ratio (100 ml) enabled the production of spherical nanospheres with a mean diameter of 285.56±0.12 nm, a process yield of 81.34±1.45% (w/w), the encapsulation efficiency of 74.67±2.13% (w/w) and drug loading of 19.76± 0.13% (w/w) [14,15].

TABLE 3: EFFECT OF AQUEOUS: OIL PHASE RATIO

Batch code	Aqueous: Oil Phase Ratio	Mean diameter [a] NM ± s.d.	Drug loading [a] (%,w/w) ± s.d.	Entrapment efficiency [a, c] (%, w/w) ± s.d.	Process yield [a, b] (%w/w) ± s.d.
P1PE-3(1:5)	1:5	700.34 ± 0.56	15.24 ± 1.56	65.87 ± 2.98	62.45 ± 2.98
P2PE -3 (1:10)	**1: 10**	**285.56 ± 0.12**	**19.76 ± 0.13**	**74.67 ± 2.13**	**81.34 ± 1.45**
P3PE -3 (1:15)	1:15	623.78 ± 2.65	16.45 ± 2.78	63.56 ± 3.67	66.56 ± 1.98

[a] Data represent the mean of three independent experiments. [b] Percentage of weight of nanospheres recovered with respect to weight of polymer utilized. [c] Percentage of encapsulated drug with respect to the total amount use.

Stirring Speed: Stirring speed plays an important role in the nanospheres size distribution and drug loading. In fact using 3:1 polymer: drug ratio and 1:10 w/o ratio and 7.5% v/v concentration of n-hexane, it was found that a 400 rpm stirring speed produced particles with rough and irregular surface. On the contrary, namely 800 rpm & 1600 rpm, led to the production of spherical nanospheres respectively, characterized by 620.21±3.45 nm, 205.68±2.46 mean diameter, 66.35±1.11% (w/w), 70.98±1.86% (w/w) process yield, drug loading 19.46±2.23% (w/w), 16.58±1.45% (w/w) and 68.55±1.02% (w/w), 69.34± 1.78 % (w/w) encapsulation efficiency. Nevertheless the vorticose motion caused by the high stirring speed led to a loss of polymer droplets out from the beaker during nanospheres production, finally resulting in a decrease of recovery [16].

The best results in term of process yield were obtained by the use of 1200 rpm stirring speed (250.34±8.56 %, w/w), nanospheres in this condition were spherical, with a 250.34±8.56 nm mean diameter, drug loading 20.36 ± 1.12% (w/w) and 72.51 ± 1.16% (w/w) encapsulation efficiency [17, 18].

TABLE 4: EFFECT OF STIRRING SPEED

Batch code	Stirring speed (rpm)	Mean diameter [a] NM ± s.d.	Drug loading [a] (%,w/w) ± s.d.	Entrapment efficiency [a, c] (%, w/w) ±s.d.	Process yield [a, b] (%w/w) ± s.d.
S1PE-3	400	900.45 ± 7.45	18.45 ± 1.06	64.73 ± 1.15	63.54 ± 1.02
S2PE -3	800	620.21 ± 3.45	19.46 ± 2.23	68.55 ± 1.02	66.35 ± 1.11
S3PE -3	**1200**	**250.34 ± 8.56**	**20.36 ± 1.12**	**72.51 ± 1.16**	**80.34 ± 1.71**
S4PE- 4	1600	205.68 ± 2.46	16.58 ± 1.45	69.34 ± 1.78	70.98 ± 1.86

[a] Data represent the mean of three independent experiments. [b] Percentage of weight of nanospheres recovered with respect to weight of polymer utilized. [c] Percentage of encapsulated drug with respect to the total amount use.

Duration of Agitation during Emulsification: For a constant speed of 1200 rpm, a polymer: drug ratio of 3:1, a w/o ratio of 1:10 and a 7.5% concentration of n-hexane, an increase of the stirring time from 1 to 4 h resulted in reduction in nanospheres size (from 945.45±1.87 to 265.67±3.98 nm). These observations could be explained by the increased shear stress generated in the emulsions associated to the increase in the duration of agitation at high homogenization rates tending to divide the droplets of the emulsions and finally inducing a decrease in the mean particle size [19]. A 4 h stirring time was chosen because the entrapment efficiency was higher (74.67±2.56%, w/w) than below 4 h (67.18±1.43%, w/w).

After optimization of the nanospheres production by single emulsion solvent evaporation technique the following condition were taken as standard:

(a) A polymer: drug ratio of 3:1 (w/w),

(b) A dispersing phase constituted of 100 ml of liquid paraffin oily solution (o/w ratio, 1:10),

(c) A concentration of 7.5% v/v of n-hexane,

(d) A stirring speed of 1200 rpm,

(e) A stirring time of 4 h.

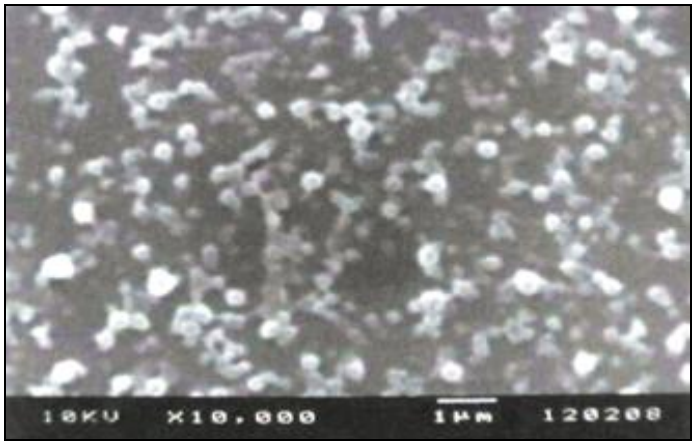
The nanospheres thus obtained were characterized by spherical shape, absence of aggregates, a mean diameter of 265.67±3.98 nm, a process yield of 83.23±1.23% (w/w), drug loading of 18.34±0.56 % (w/w) and an encapsulation efficiency of 74.67±2.56% (w/w) [20].

TABLE 5: EFFECT OF DURATION OF AGITATION DURING EMULSIFICATION:

Batch code	Stirring Time	Mean diameter [a] NM ±s.d.	Drug loading [a] (%,w/w) ± s.d.	Entrapment efficiency [a, c] (%, w/w) ± s.d.	Process yield [a, b] (%w/w) ± s.d.
T1PE-3	1 hr	945.45 ± 1.87	15.67 ± 1.90	65.23 ± 2.78	63.98 ± 1.09
T2PE -3	2 hr	658.24 ± 3.09	16.78 ± 2.98	68.89 ± 1.98	68.34 ± 2.67
T3PE -3	3 hr	345.89 ± 2.08	16.89 ± 0.98	69.67 ± 1.78	73.12 ± 0.34
T4PE-3	**4 hr**	265.67 ± 3.98	18.34 ± .56	74.67 ± 2.56	83.23 ± 1.23

[a] Data represent the mean of three independent experiments. [b] Percentage of weight of nanospheres recovered with respect to weight of polymer utilized. [c] Percentage of encapsulated drug with respect to the total amount use.

Scanning Electron Microscopic Studies: The spherical shape of nanospheres was established by SEM. The surface analysis of drug loaded nanospheres prepared by the w/o single emulsion solvent evaporation method revealed that the nanospheres were spherical and polydispersed with a diameter of 265.67 ± 3.98 nm. The surface of these nanospheres was found to be smooth with quite a few pock marks. This probably happens due to slow release of acetone and methanol during the terminal stage of the evaporation process [21].



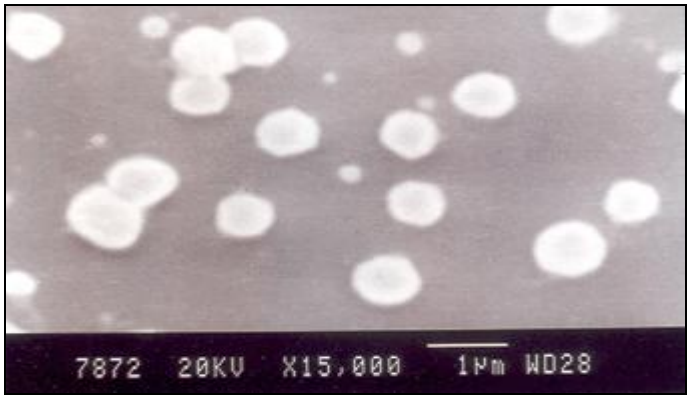


FIGURE 1: SEM IMAGES OF OPTIMIZED BATCH (FPE-3) OF PROPANOLOL HYDROCHLORIDE NANOSPHERES

Particle Size Analysis: The particle size analysis of different formulations was done by Malvern Zeta Size analyzer [22]. The FPE-3 formulation showed best results in term of mean diameter 250.34±8.56 nm mean diameter.

Drug Excipients Compatibility: FTIR technique was used to check the compatibility drug excipients. IR spectra of Propranolol hydrochloride (**Fig. 4.8**) showed peaks at 2965 cm^{-1}, 3283 $cm^{-1,}$ 1267 cm^{-1} and

798 cm^{-1} respectively showing the presence of secondary amine group, hydroxyl group (secondary), Alkyl aryl ether stretching band and substituted naphthalene group. IR spectra of Drug + Eudragit RS100 + Eudragit RL 100 [23] (**Fig. 2**) showed the relative peaks 2965 cm^{-1}, 1267 cm^{-1} and 798 $cm^{-1}$of functional groups of drug. Thus it indicated that drug and polymers compatible to each other for nanospheres formulation.

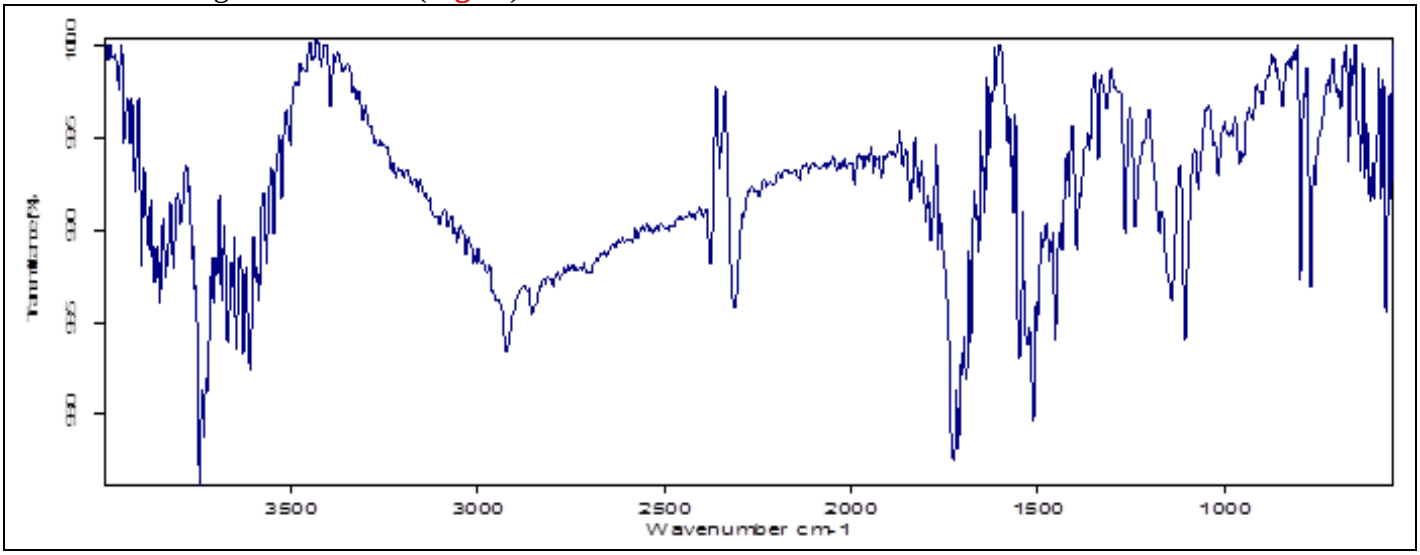


FIGURE 2: FTIR PATTERN OF PURE DRUG (PROPANOLOL HYDROCHLORIDE), EUDRAGIT RL 100 AND EUDRAGIT RS 100

***In-vitro* Drug Release studies:** *In vitro* Propranolol Hydrochloride release studies from Eudragit RS 100 nanospheres were performed in pH 7.4 phosphate buffer at 37 ± 0.5°C. Propranolol hydrochloride release from the nanospheres was found to be slow and spread over extended period of time (24 h). Percent of Propranolol hydrochloride released from the nanospheres was decreased with an increase in coat material in the nanospheres (p<0.05). The increased density of the polymer matrix at higher concentrations results in an increased diffusional path length. This may decrease the overall drug release from the polymer matrix [24]. Furthermore, smaller nanospheres are formed at a lower polymer concentration and have a large surface area exposed to dissolution medium, giving rise to faster drug release. The dissolution profiles of the nanospheres could be divided into three stages [25, 26].

In this study, drug dissolution profiles are shown in **Fig. 4.12**. The dissolution profiles of different formulations (PE-1, PE-2, PE-4 and PE-5) of nanospheres showed 94.12, 90.21, 78.64, 72.35% cumulative release respectively. The final optimized drug formulation FPE-3 (polymer: drug ratio (3:1), stirring speed (1200 rpm), stirring time (4h), phase ratio (1:10)) showed 8.92 % cumulative release in few minutes. After 24 hrs showed 85.42% cumulative release.

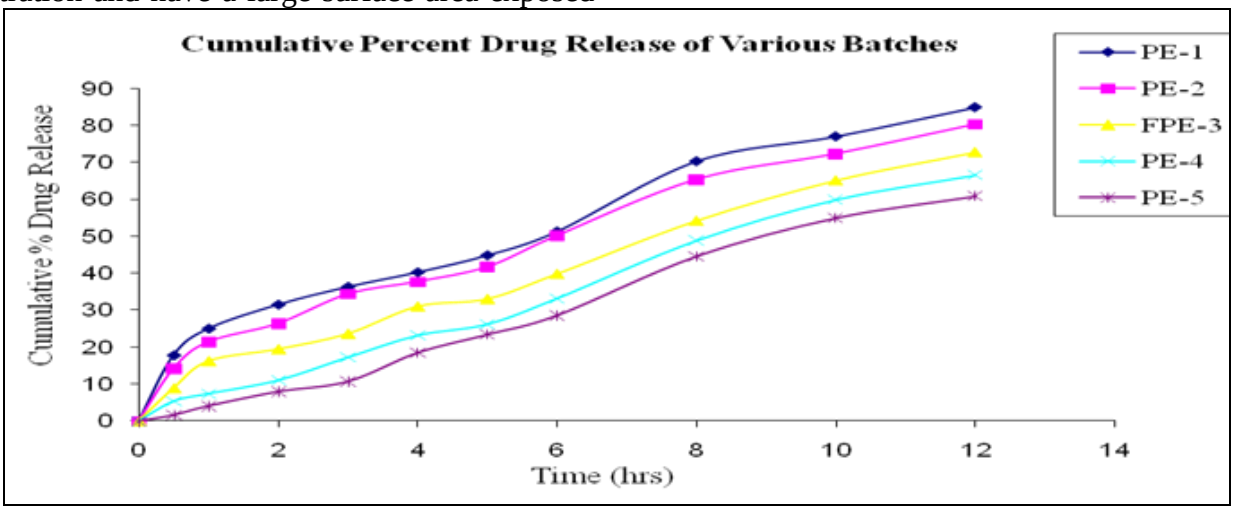


FIGURE 3: CUMULATIVE PERCENT DRUG RELEASE OF VARIOUS BATCHES

Kinetics of Drug Release: In order to investigate the release mechanism of present drug delivery system, the data obtained from *in vitro* release of final optimized batch (FPE-3) were fitted into equations for the zero-order, first-order, and Higuchi release model and Peppas equation [27]. T

he interpretation of data was based on the values of the resulting regression coefficients. The in vitro drug release showed the regression coefficient values for Higuchi's model (**Fig. 4.13**) (R^2= 0.9051), Korsmeyer Peppas model (Fig. 4.14) (R^2= 0.954), First order plot (**Fig. 4.15**) (R^2= 0.97) and zero order plot (**Fig. 4.16**) (R^2= 0.985).

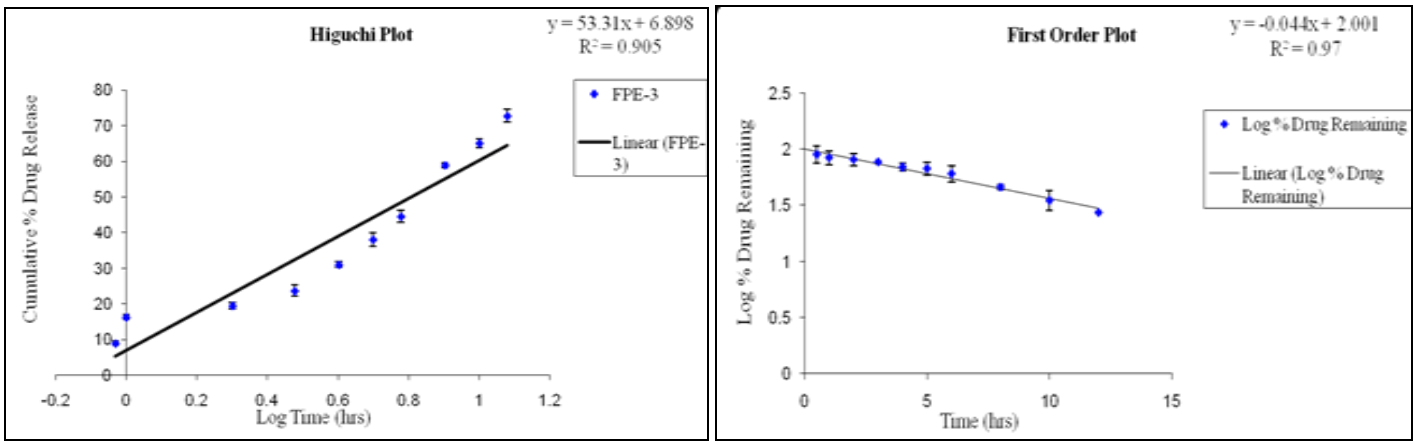


FIGURE 4(A): HIGUCHI PLOT (B) FIRST ORDER PLOT OF OPTIMIZED BATCH (FPE-3) OF PROPANOLOL HYDROCHLORIDE NANOSPHERES

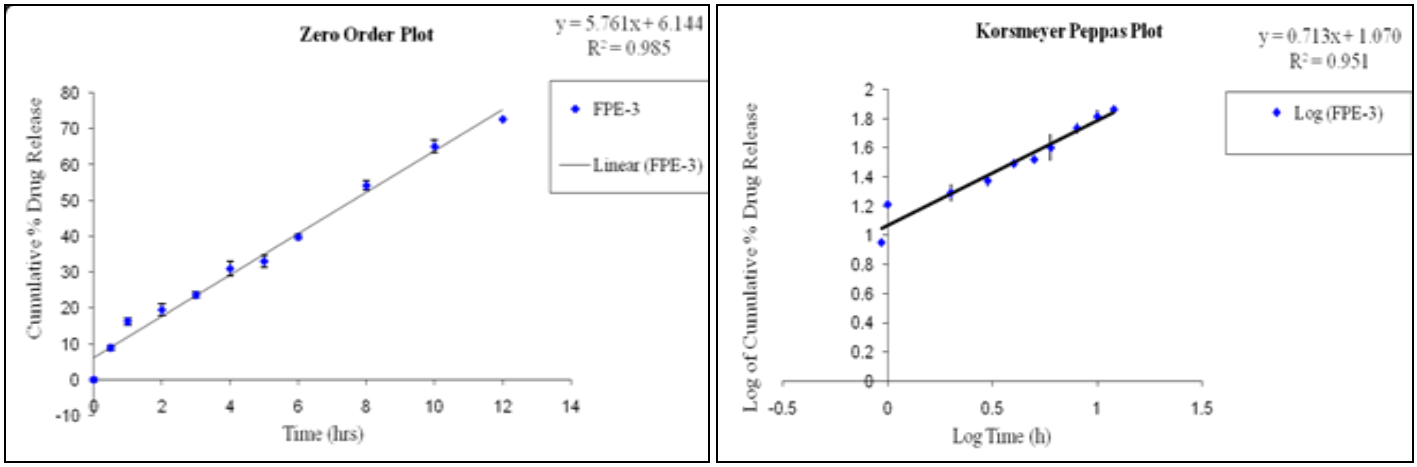


FIGURE-5:(A) ZERO ORDER PLOT (B) KORSMEYER PLOT OF OPTIMIZED BATCH (FPE-3) OF PROPANOLOL HYDROCHLORIDE NANOSPHERES

Storage Stability: Propranolol Hydrochloride nanospheres in the form of lyophilized powder were stored in glass bottles at 4±1°C, room temperature and 40±1°C, 75% RH for period of 3 months and evaluated for any change in the shape and structural integrity by microscopic examination and residual drug content.

At 40±1°C, agglomerates of nanospheres were found after storage for three months, which may be attributed to polymer softening and fusion. Optimal storage condition of the formulation was assessed by analyzing the residual drug content after the time intervals of 15, 30, 45, 60 and 90 days [28].

The percent residual drug content was determined and found to be 96.12±0.13 and 95.23±0.22 at 4±1°C and room temperature respectively after storage for 90 days. The log percent residual drug content was plotted against time (t) (**Figure 5(a) and 5(b)**), which reflected an almost linear relationship. *k* (degradation rate constant) was calculated from which the time required for 10% drug leaching was calculated [29].

Nanospheres formulation stored at 4 ± 1°C showed the *k* value as 1.534×10^{-4} and $t_{10\%}$ value of nearly 686 days, while those stored at room temperature showed the *k* value as 4.145×10^{-4} and $t_{10\%}$ value of nearly 254 days.

The $t_{10\%}$ obtained in case of formulation stored at room temperature were found lower in comparison with the formulations stored at 4±1˚C which indicated that the formulations tend to degrade faster at higher temperatures [30, 31].

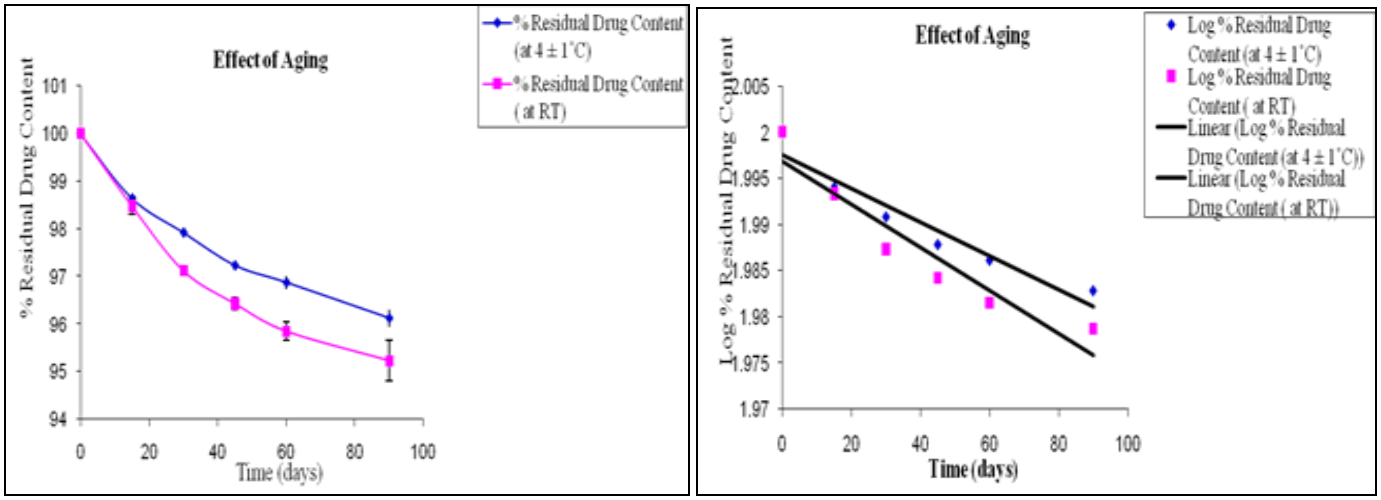


FIGURE 6: EFFECT OF AGING ON (A) % RESIDUAL CONTENT AT 4 ± 1˚C (B) LOG % RESIDUAL CONTENT AT 4 ± 1˚C OF OPTIMIZED FORMULATION (FPE-3) OF NANOSPHERES.

Statistical analysis: Statistical data analyses were performed using the Student's t-test and one-way analysis of variance (ANOVA) with $p < 0.05$ as the minimal level of significance [32].

CONCLUSION: Single emulsion solvent evaporation method was used to prepare nanospheres of Propranolol Hydrochloride. These investigations have also provided an understanding of the effects of some process parameters on particle size and shape, and encapsulation efficiency, drug loading and process yield The investigated system has the potential to remain in treated site for a prolonged periods and capable of maintaining constant concentration of drug through a longer duration of time due to its sustained action, this can be expected to reduce the frequency of administration and decrease the dose dependent side effects associated with repeated administration of conventional Propranolol Hydrochloride loaded dosage forms, which ultimately improve patient compliance.

Single emulsion solvent evaporation method were suitable for the preparation of nanospheres in the mean diameter mean diameter of 265.67 ± 3.98 nm, a process yield of 83.23 ± 1.23% (w/w), drug loading of 18.34 ± 0.56 % (w/w) and an encapsulation efficiency of 74.67 ± 2.56% (w/w). It concluded that sustained release Propranolol Hydrochloride nano-spheres were successfully prepared by using single emulsion solvent evaporation method with the selection of appropriate experimental conditions.

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