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FORMULATION DESIGN AND IN VITRO EVALUATION OF TAMOXIFEN NANOSPONGES

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ABSTRACT

The pharmaceutical and health care industry has been creating and using nano-scale materials for resolving many physical, biological and chemical problems related with the treatment of disease. The hydrophobic nature of most of the drugs presents a challenge for effective in vivo delivery. Shrinking materials to nano size has profoundly enhanced the efficacy of such drugs. An ideal drug therapy attains effective drug concentration at the target site for a specified period of time and minimizes general and local side effects. To obtain a desirable therapeutic response, the correct amount of drug should be transported and delivered to the site of action with subsequent control of drug input rate. Nanosponges are made of microscopic particles with few nanometers wide cavities, in which a large variety of substances can be encapsulated. These particles possess the ability to carry both lipophilic and hydrophilic substances and thereby improving the solubility of poorly water soluble molecules. The studies conducted in this field proves that the tiny mesh-like structures called nanosponges may revolutionise the treatment of many diseases and early trials suggest this technology is up to five times more effective at delivering drugs for breast cancer than conventional methods.

INTRODUCTION

The nanosponges are encapsulating type of nanoparticles which encapsulates the drug molecules within its core. Based on the method of associating with drugs, the nanoparticles are classified into encapsulating nanoparticles, conjugating nanoparticles and complexing nanoparticles.

Targeting Sites by Nanosponges

"Tagging" drug-loaded nanosponges ensures desired pharmacological response by targeting only disease affected cells and leaving the healthy ones unharmed. Drugs encapsulated within the nanosponge pores are shielded from premature destruction and stability of drug is enhanced. This tiny sponge circulates around the tumour cell until they encounter the surface to release their drug cargo in a sustained manner. Nanosponge is three to five times more effective at decreasing tumour growth than direct injection. The targeted delivery systems of nanosponge have several basic advantages like, the drug is released at the tumour instead of circulating widely through the body, and it is more effective for a given dosage. The nanosponges have basic features such as fewer harmful side effects as smaller amounts of the drug will come into contact with healthy tissue.

Characteristic Features of Nanosponges

- Nanosponges of specific size can be synthesized by changing the crosslinker to polymer ratio.
- They are nontoxic, porous particles, insoluble in most organic solvents and stable up to 300^0C. They are stable at the pH range of 1-11.
- They form clear and opalescent suspension in water.
- They can be reproduced by simple thermal desorption, extraction with solvents, by using microwaves and ultrasounds.
- Their three-dimensional structure allows capture, transportation and selective release of a variety of substances.
- Chemical linkers permit nanosponges to bind preferably to the target site.
- By complexing with different drugs nanosponges can form inclusion and non-inclusion complexes.
- By adding magnetic particles into the reaction mixture, magnetic properties can also be imparted to nanosponges.

Polymers Used in Nanosponges Preparation

There are various polymers and cross linkers are used in the preparation of nanosponges. **Polymers:** Hyper cross linked Polystyrenes, Cyclodextrines and its derivatives like Alkyloxycarbonyl Cyclodextrins, Methyl β-Cyclodextrin, Hydroxy Propyl β-Cyclodextrins. **Copolymers:** Poly (valerolactoneallylvalerolactone), Poly (valerolactoneallylvalerolactone oxepanedione), Ethyl Cellulose, Poly vinyl alcohol. **Cross linker:** Carbonyl diimidazoles, Carboxylic acid dianhydrides, Diarylcarbonates, Dichloromethane, Diisocyanates, Diphenyl Carbonate, Epichloridine, Gluteraldehyde,

Pyromellitic anhydride, 2,2-bis (acrylamido)Acetic acid.

Preparation of Nanosponges

Nanosponges are prepared mainly on the criteria of delivery system,polymer and nature of drug and solvents

1. Nanosponges prepared from hyper-cross linked β-cyclodextrins
2. Emulsion solvent diffusion method
3. Quasi-emulsion solvent diffusion
4. Ultrasound- Assisted Synthesis

Loading of Drug Into Nanosponges

Suspend the prepared nanosponges in water and sonicate to avoid the presence of aggregates and then centrifuge the suspension to collect the colloidal fraction.Separate the supernatant and then dry the sample by freeze drying. The aqueous suspension of nanosponges was prepared and dispersed the amount of the drug to be loaded in it. Maintain the suspension under constant stirring for specific time required for complexation. After complexation, separate the uncomplexed (undissolved) drug from complexed drug by centrifugation. Then obtain the solid crystals of nanosponges by solvent evaporation or by freeze drying.

Marketed Formulations

Table 1: Marketed formulations of nanosponges.

Drug	Administration Route	Trade Name	Dosage Form
Dexamethasone	Dermal	Glymesason	Tablet
Iodine	Topical	Mena- gargle	Solution
Alprostadil	I.V	Prostavastin	Injection
Piroxicam	Oral	Brexin	Capsule

LITERATURE REVIEW

- *Priyanka et al (2018)* formulated ibuprofen loaded nanosponges for topical application. Emulsion solvent diffusion method was selected to prepare ibuprofen loaded nanosponges using different rations of drug: polymer. The obtained nanosponges have been evaluated for physiochemical characteristics and in vitro release studies. The shape and morphology of drug loaded nanosponges were investigated and confirmed by SEM. FTIR results were in agreement with standard spectral studies and moreover it was identified that there was no intraction between drug and polymer. Entrapment efficiency of the NS was found to be around 70.41%. The production yield and in vitro release studies was also good. Overall this study resulted in porous nature of nanosponges which provides a channel for the release of the drug and the method is quick and reproducible.
- *Sornsuvit et al (2018)* aimed to determine the pharmacokinetic parameters and bioavailability of silymarin 140mg self micro-emulsifying drug delivery system (SMEDDS) formulation. An open label, single-dose pharmacokinetic study was conducted. Twelve healthy volunteers were included in the study. After the volunteers had fasted overnight for 10 h, a single-dose generic silymarin 140mg SMEDDS soft capsule was administered. Then 10ml blood sample were taken at 0.0, 0.25, 0.50, 0.75, 1.0, 1.33, 1.67, 2.0, 2.5, 3.0, 4.0, 6.0, 8.0, 10.0, and 12.0 h. The plasma silymarin concentration were analysed using validated LC-MS/MS. The pharmacokinetic parameters were analysed and calculated.

AIM AND OBJECTIVE

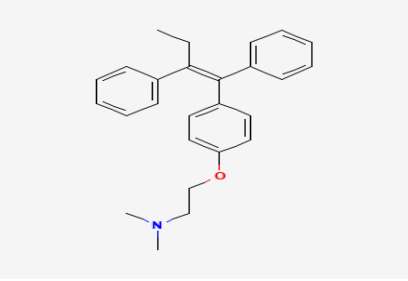
- To formulate Tamoxifen nanosponges so as to target cancer cells particularly breast cancer, colorectal cancer using different polymers.
- To increase the bioavailability of Tamoxifen by developing Tamoxifen nanosponges.
- To reduce the dose, dosing frequency and to reduce dose dependent side effects of Tamoxifen.
- To facilitate drug targeting or selective uptake of drug.
- Deliver the drug at specified site in a controlled manner without showing any burst effect.

To achieve the objective the following steps were carried out

- The preformulation studies.
- Formulation of Tamoxifen nanosponges by general full factorial design.
- Characterization of prepared Tamoxifen nanosponges.
- In-vitro evaluation of Tamoxifen nanosponges.

DRUG PROFILE

DRUG NAME: Tamoxifen



Uses: Bladder carcinoma, breast cancer, Gastric cancer, Gynecological carcinoma.

EXCIPIENTS

EUDRAGIT® E 100, EUDRAGIT® E PO, EUDRAGIT® E 12,5, ETHYL CELLULOSE

RESULTS AND DISCUSSION

I. PREFORMULATION STUDIES Physical Characteristics

Tamoxifen was checked for its colour, odour and texture. Tamoxifen is red coloured powder in appearance, odourless and amorphous in nature.

Solubility

Solubility test for Tamoxifen was carried out in different solvents such as ethanol, water, dichloromethane and chloroform and results are given in Table 1.

Table 1: Solubility test for Tamoxifen in different solvents.

Sl. No	Solvent	Soluble	Sparingly Soluble	Insoluble
1.	Ethanol	□	-	-
2.	Dichloromethane	□	-	-
3.	Chloroform	-	□	-
4.	Water	□	-	-

Selection of Wavelength

The Tamoxifen stock solution of concentration 100µg/mL was scanned in the range of 200- 400nm for λ_{max}. using double beam UV Spectrophotometer. The absorption peak obtained is shown in Figure 1.

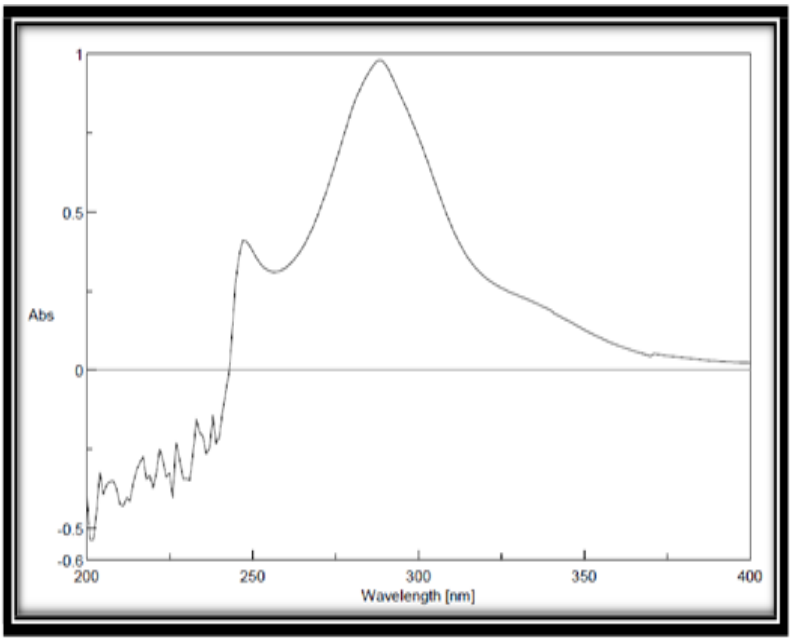


Figure 1: UV spectra of Tamoxifen.

The maximum absorption of Tamoxifen was found to be at 232nm and hence it is selected as the wavelength for further studies.

Construction of calibration curve of Tamoxifen

In the calibration curve, linearity was obtained between 5-40 µg/ml concentration of Tamoxifen and the regression value was found to be $r^2 = 0.9996$. Hence we can conclude that Tamoxifen obeys Beer Lambert's Law at the concentration between 5-40 µg/ml. The results are shown in Table 2 and Figure 5.

Table 2: Concentration and absorbance values for estimation of Tamoxifen.

Sl. No	Concentration (µg/ml)	Absorbance (AU) at 232nm
1.	5	0.1686
2.	10	0.3624
3.	15	0.5357
4.	20	0.6963
5.	25	0.8770
6.	30	1.0693
7.	35	1.2700
8.	40	1.4516

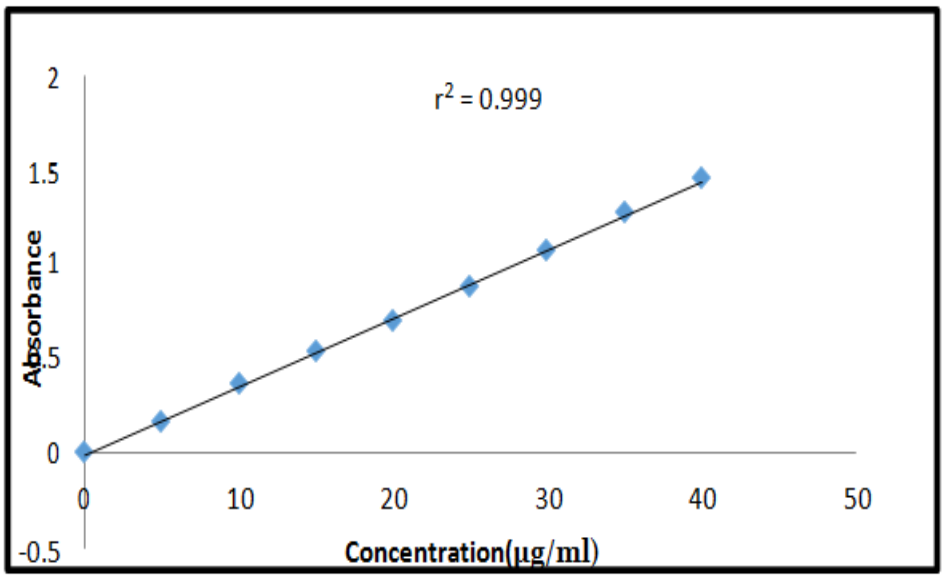


Figure 2: Calibration graph of Tamoxifen.

Excipient Compatibility Studies

Fourier Transform Infrared (FT-IR) spectra of the samples were obtained using a SHIMADZU Spectrometer by KBr disc method. The spectrums were recorded for the pure drug and physical mixture of drug and polymer and are shown in Figures 3,4, and 5.

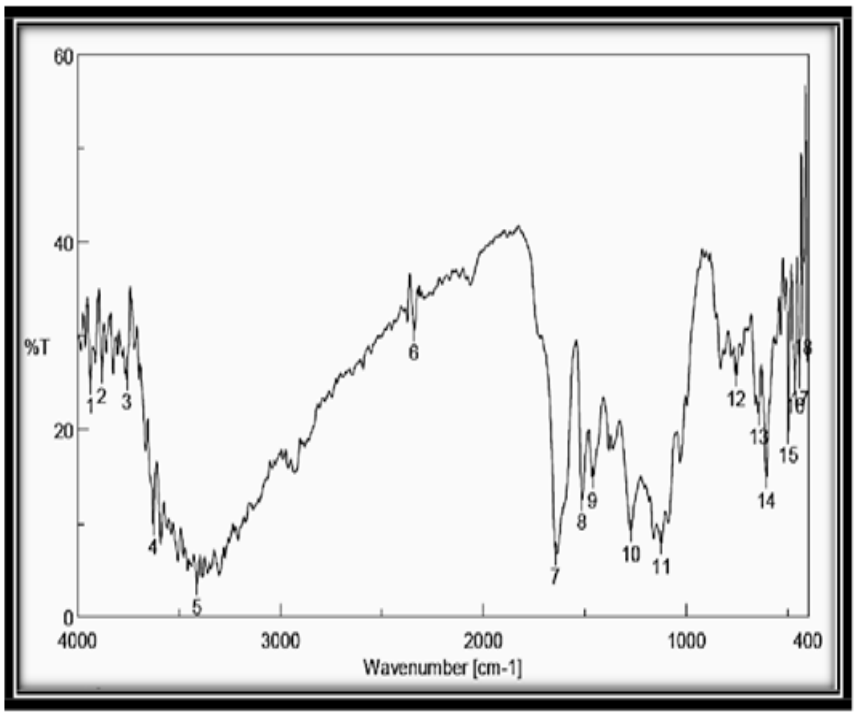


Figure 3: FTIR – spectrum of Tamoxifen.

Table 3: FTIR interpretation of Tamoxifen.

Materials	Standard wave number (cm-1)	Test wave number (cm-1)	Functional group assignment
Tamoxifen	3650-3200	3410.49 3625.52	OH stretching
	1820-1665	1643.05	C=O stretching
	1320-1210	1273.75	C-O-C stretching
	1161-1029	1121.4	In plane=C-H bending

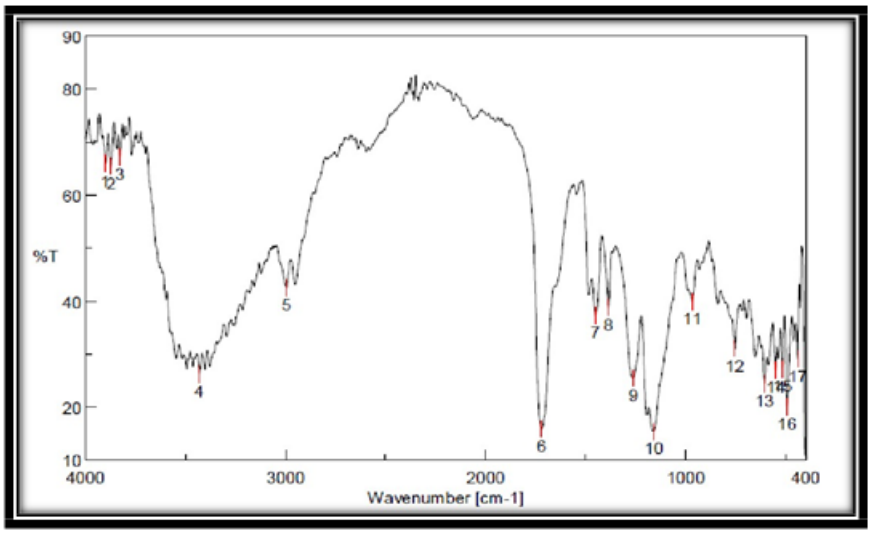


Figure 4: FTIR spectrum of Eudragit.

Table 4: FTIR interpretation of Eudragit.

Materials	Standard wave number(cm-1)	Test wave number (cm-1)	Functional group assignment
EUDRAGIT	3000-3700	3430.74	O-H stretching
	1500-1800	1720.19	N-H bending
	2700-3300	2995.87	C-H stretching
	1300-1500	1451.17 1386.57	C-H bending
	1000-1300	1262.18 1159.01	C-O stretching

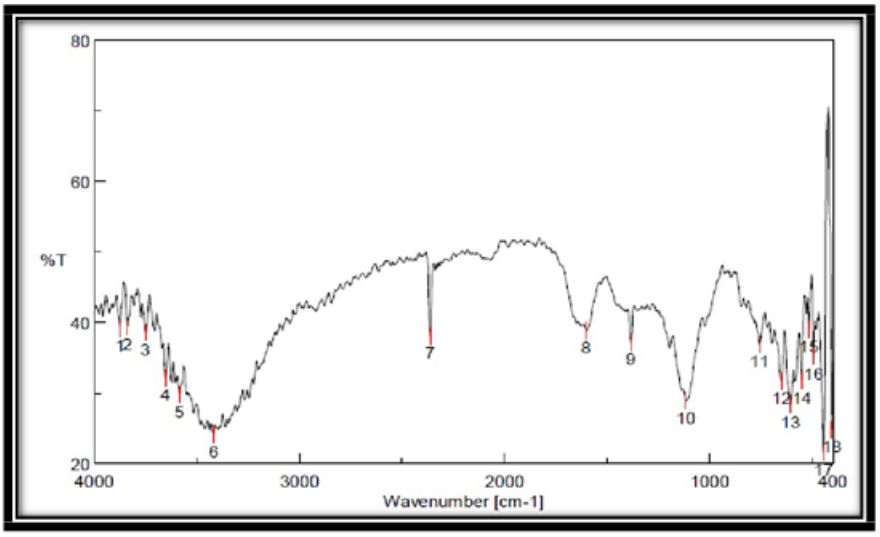


Figure 5: FTIR spectrum of Poly Vinyl Alcohol (PVA).

Table 5: FTIR interpretation of Poly Vinyl Alcohol.

Materials	Standard wave number(cm-1)	Test wave number(cm-1)	Functional group assignment
POLYVINYL ALCOHOL	3300-3600	3584.06	OH stretching
	2850-2970	2862.37	CH_3 stretching
	1500-1760	1600.63	COOH
	1340-1470	1383.68	Alkanes bending
	1000-1300	1116.58	C-O stretching
	600-800	757.888 648.929	C-H rocking

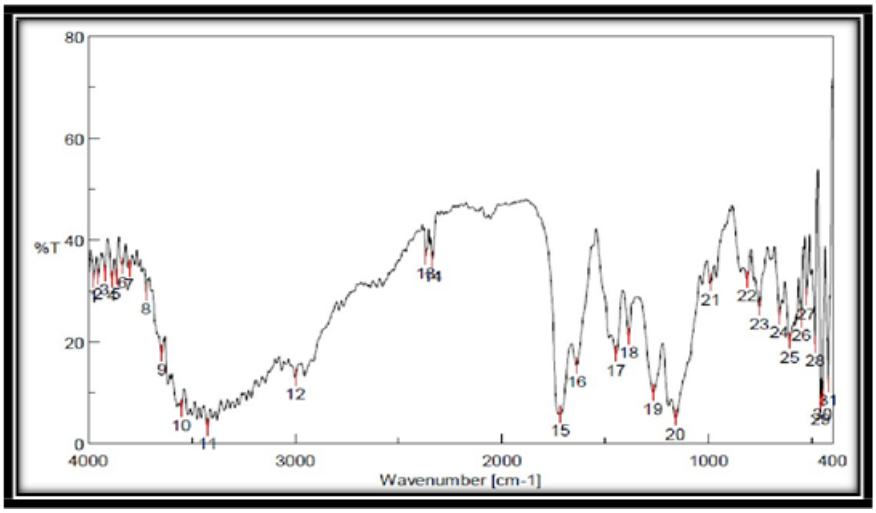


Figure 6: FTIR spectrum of physical mixture containing Tamoxifen, Eudragit and PVA.

Table 6: FTIR interpretation of mixture containing Tamoxifen, Eudragit and PVA.

Materials	Standard wave number (cm-1)	Test wave number (cm-1)	Functional group assignment
	3650-3200	3642.87 3423.033	OH stretching
	3300-2700	2999.73	C-H stretching
MIXTURE	1820-1665	1718.26	C=O stretching
CONTAINING	1800-1500	1639.2	N-H bending
IDARUBICIN,	1500-1300	1386.57	C-H bending
EUDRAGIT and	1320-1210	1268.93	C-O-C stretching
PVA	1161-1029	1161.9	In plane bending =C-H
	800-600	814.777 658.571	C-H rocking

The peaks present in the FTIR spectra of pure Tamoxifen are present in the FTIR spectra of physical mixture containing Tamoxifen with ethyl cellulose and Tamoxifen with eudragit. It is therefore evident that the Tamoxifen is compatible with the excipients ethyl cellulose eudragit and poly vinyl alcohol and can be chosen for the formulation of Tamoxifen nanosponges.

II. FORMULATION OF NANOSPONGES

Selection of polymers for the formulation of Tamoxifen nanosponges by emulsion solvent diffusion method was based on the trial batches carried out by using different polymers such as ethyl cellulose, eudragit, sodium alginate, HPMC, Carbopol, hydroxyl ethyl cellulose, chitosan and pectin and details are depicted in table 15. Drug: polymer ratio was selected based on the literature. The results indicated that ethyl cellulose and eudragit was found to be suitable for the formulation of Tamoxifen nanosponges.

Table 7: Trial batches for formulation of Tamoxifen nanosponge.

Drug	Polymer	Ratio	Result observed
TAMOXIFEN	Ethyl cellulose	1:2	Product obtained
	Eudragit	1:2	Product obtained
	Hydroxy propyl methyl cellulose	1:2	Less yield
	Hydroxyl ethyl cellulose	1:2	Less yield
	Carbopol	1:2	Gel like product
	Sodium alginate	1:2	Gel like product
	Chitosan	1:2	No product
	Cyclodextrin	1:2	No product
	Pectin	1:2	No yield

Total ten formulations (F1 – F5 and F6 – F10) of Tamoxifen nanosponges with two different polymers ethyl cellulose and eudragit in different ratios were formulated by emulsion solvent diffusion method as given in Table 16 and Table 17.

Table 8: Formulation of Tamoxifen nanosponges.

S. No	Formulation code	Drug	Polymer	Drug: polymer ratio
1	F1	TAMOXIFEN	Ethyl cellulose	1:0.5
2	F2		Ethyl cellulose	1:1
3	F3		Ethyl cellulose	1:1.5
4	F4		Ethyl cellulose	1:2
5	F5		Ethyl cellulose	1:3
6	F6		Eudragit	1:0.5
7	F7		Eudragit	1:1
8	F8		Eudragit	1:1.5
9	F9		Eudragit	1:2
10	F10		Eudragit	1:2.5

Table 9: Formulation of Tamoxifen nanosponges by emulsion solvent diffusion technique.

S. No	Formulation code	Weight of drug (mg)	Weight of polymer (mg)	Weight of polyvinyl alcohol (mg)
1	F1	100	50	200
2	F2	100	100	200
3	F3	100	150	200
4	F4	100	200	200
5	F5	100	300	200
6	F6	100	50	200
7	F7	100	100	200
8	F8	100	150	200
9	F9	100	200	200
10	F10	100	250	200

III. Characterisation of Tamoxifen Nanosponges

FTIR Spectroscopy of Tamoxifen nanosponges

FTIR Spectrum of Tamoxifen nanosponges using ethyl cellulose is given in figure 7.

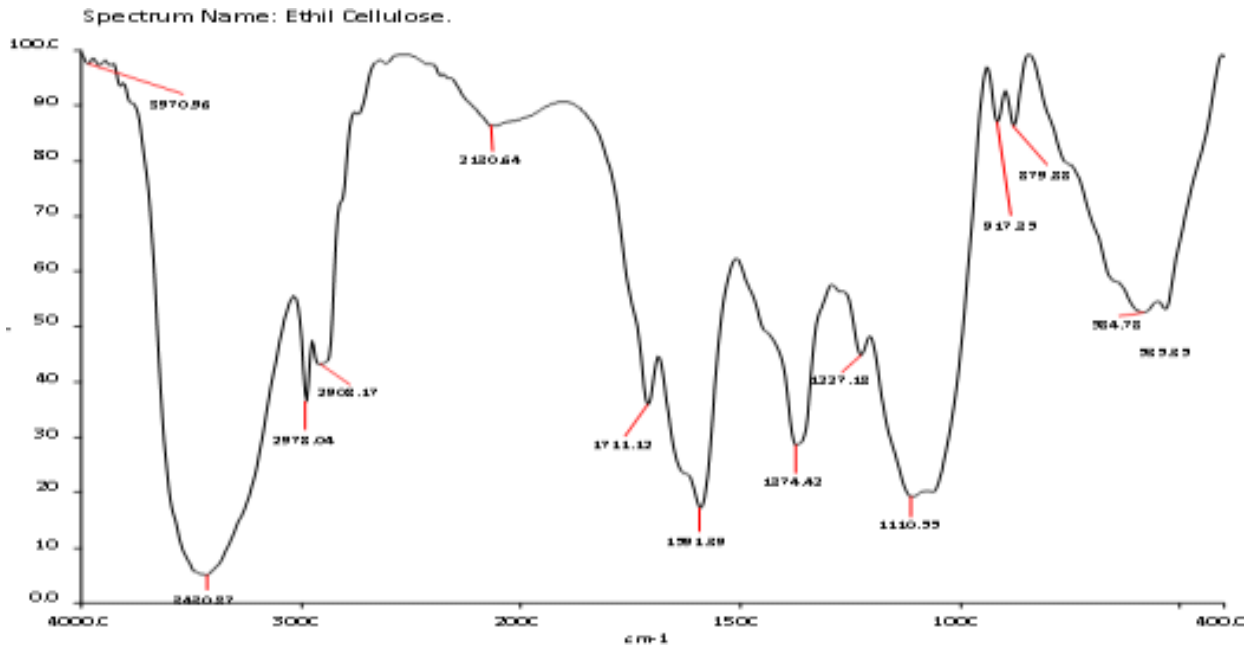


Figure 7: FTIR interpretation of Tamoxifen nanosponges using Ethyl cellulose Table 10: FTIR interpretation of Tamoxifen nanosponges using Ethyl cellulose.

FTIR Spectroscopy of Tamoxifen Nanosponges

FTIR spectrum of Tamoxifen nanosponge using eudragit is given in Figure 8.

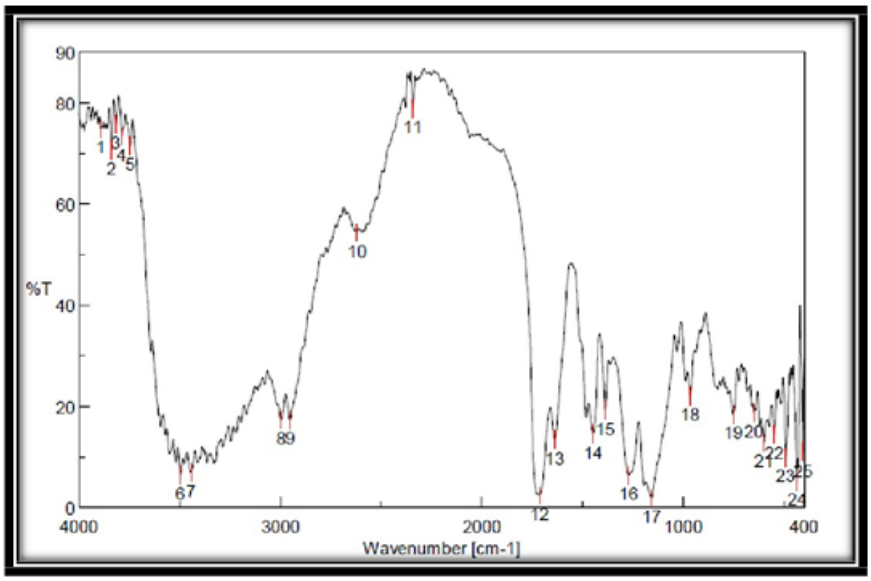


Figure 8: FTIR spectrum of Tamoxifen nanosponges using Eudragit.

Table 12: FTIR interpretation of Tamoxifen nanosponges using Eudragit.

Materials	Standard wave number(cm-1)	Test wave number(cm-1)	Functional group Assignment
FORMULATION F9	3650-3200	3497.27 3444.24	OH stretching
	3300-2700	2993.94 2951.52	C-H stretching
	1820-1665	1714.41	C=O stretching
	1800-1500	1638.23	N-H bending
	1500-1300	1449.24	C-H bending
	1320-1210	1271.82	C-O-C stretching
	1161-1029	1159.01	In plane =C-H Bending
	800-600	753.066 648.929	C-H rocking

The peaks present in the FTIR spectra of pure Tamoxifen are present in the FTIR spectra of formulations. The FTIR interpretations indicated that the Tamoxifen is compatible with the excipients eudragit and poly vinyl alcohol and no interactions observed in all formulations of nanosponges.

Percentage yield analysis

Percentage yield of the formulated Tamoxifen nanosponges were calculated using the formula:

$$Percentage\ Yeild = \frac{Practical\ yield}{Theoritical\ yield} \times 100$$

Table 13: Percentage yield of Tamoxifen nanosponges.

S. No	Formulation code	Percentage yield (%)
1.	F1	65.76
2.	F2	71.25
3.	F3	73.28
4.	F4	78.16
5.	F5	80.34
6.	F6	32.08
7.	F7	34.14
8.	F8	48.57
9.	F9	49.75
10.	F10	57.22

The percentage yield was minimum for formulation F6 (32.08%) and maximum for formulation F5 (80.34%). From the results we can conclude that as the concentration of polymer increases the percentage yield also increases. It can also be noted that the yield obtained while using ethyl cellulose as polymer is much higher when compared with eudragit. The percentage yield of all formulations is depicted in Figure 9.

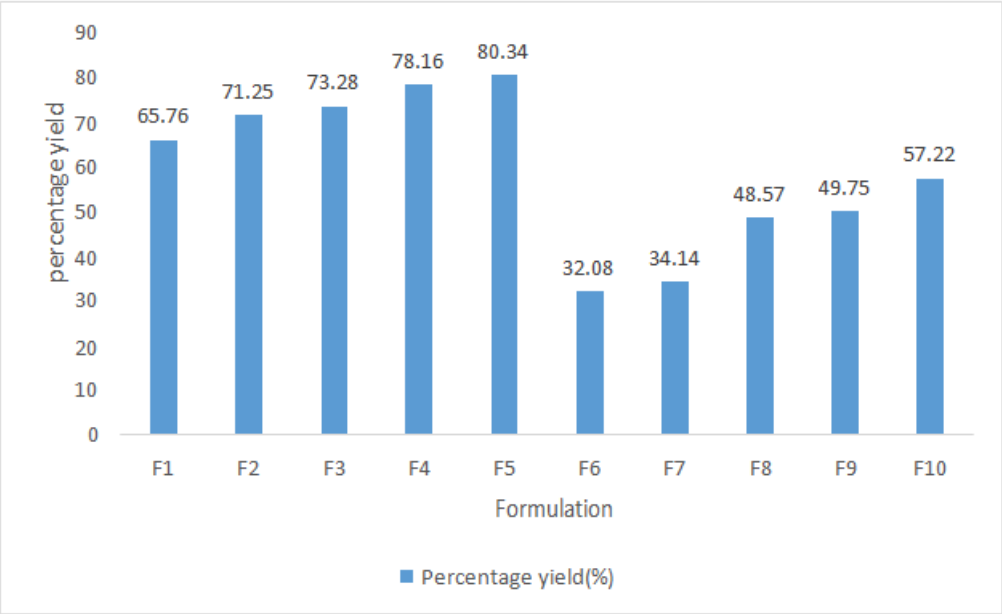


Figure 9: Percentage yield analysis of Tamoxifen nanosponges.

Scanning Electron Microscopy

SEM analyses of the formulated Tamoxifen nanosponges were performed to evaluate the surface morphology of nanosponges. The SEM images of formulation F9 are shown in Figure 10.

SEM images showed the nanosponge was porous with a smooth surface morphology and spherical in shape. The spongy and porous nature of the nanosponges can be seen in the above figures. The presence of pores was due to the impression of diffusion of the solvent dichloromethane.

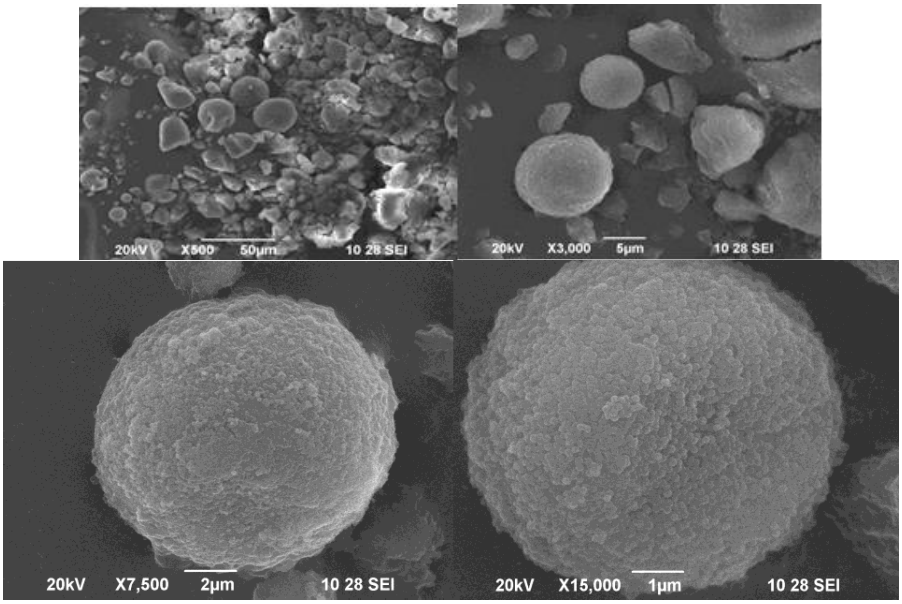


Figure 10: SEM images of Tamoxifen nanosponges using eudragit.

Particle Size Measurement

The particle size is one of the most important parameter for the characterisation of nanosponges. The average particle sizes of the prepared Tamoxifen nanosponges were measured using Malvern zeta sizer.

Particle size analysis showed that the average particle size of Tamoxifen nanosponges formulated using eudragit (F9) was found to be 4097 nm with polydispersity index (PDI) value 1.00 and with intercept 1.41. The zeta size distribution of ethyl cellulose –Tamoxifen nanosponges is depicted in Figure 11.

			Size (d.nm):	% Intensity:	St Dev (d.n...
Z-Average (d.nm):	1.708e4	Peak 1:	1.117	100.0	1.490e-8
PdI:	0.767	Peak 2:	0.000	0.0	0.000
Intercept:	1.46	Peak 3:	0.000	0.0	0.000
Result quality :	Refer to quality report				

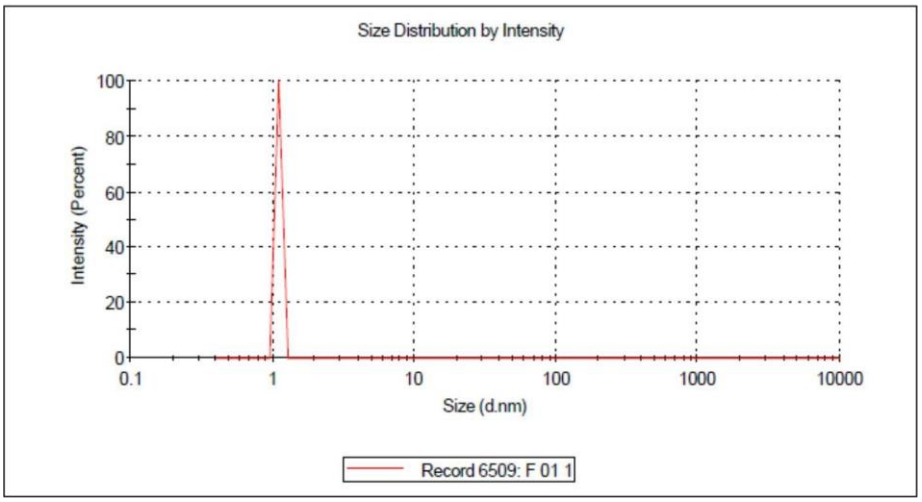


Figure 11: Zeta size distribution of Tamoxifen nanosponges.

The average particle size analyses of eudragit-Tamoxifen nanosponges are 1.708which is lesser than 5µm.

Determination of Zeta Potential

Zeta Potential was determined using Malvern zeta-sizer instrument. Zeta potential analysis is carried out to find the surface charge of the particles to know its stability during storage. The magnitude of zeta potential is predictive of the colloidal stability. Nanoparticles with zeta potential value greater than +25 mV or less than -25 mV typically have high degrees of stability.

For Tamoxifen nanosponges using eudragit zeta potential was found to be -24.3mV with peak area of 100% intensity. These values indicate that the formulated Tamoxifen nanosponges are stable. Zeta potential distribution of Tamoxifen nanosponges prepared using eudragit is depicted in Figure 12.

			Mean (mV)	Area (%)	St Dev (mV)
Zeta Potential (mV):	-24.3	Peak 1:	-24.3	100.0	6.96
Zeta Deviation (mV):	6.96	Peak 2:	0.00	0.0	0.00
Conductivity (mS/cm):	0.0111	Peak 3:	0.00	0.0	0.00
Result quality :	Good				

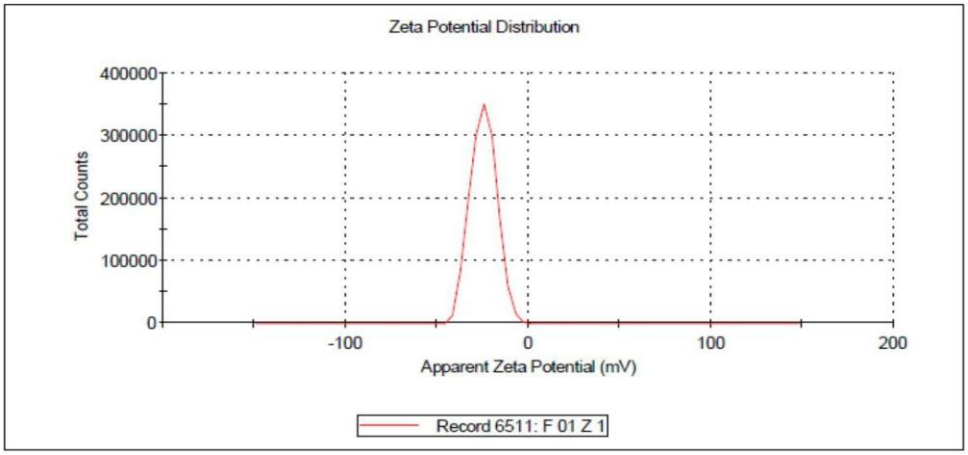


Figure 12: Zeta potential of Tamoxifen nanosponges Entrapment efficiency.

The amount of entrapped drug was calculated from the equation:

$$\% \ Drug \ Entrpment = \frac{Practical \ drug \ content}{Theoretical \ drug \ content} \times 100$$

Entrapment efficiency of prepared formulation is given in Table 14 and Figure 13.

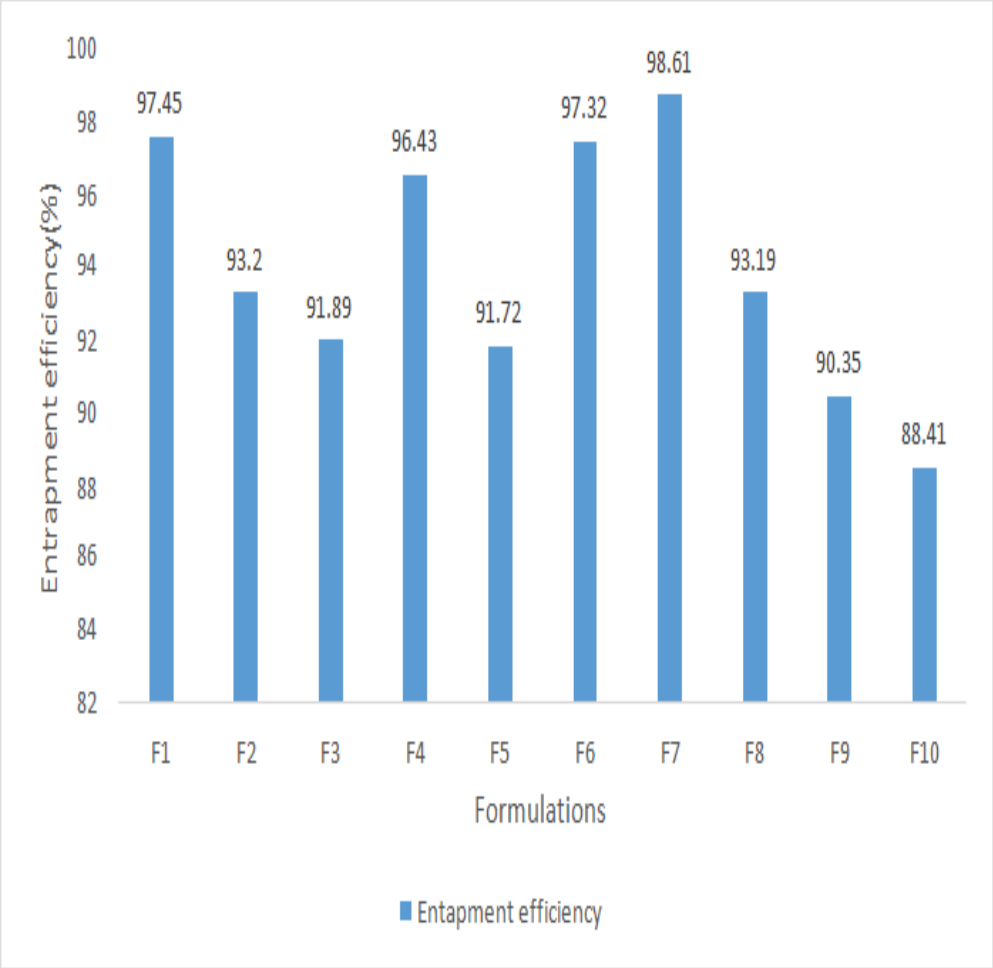


Figure 13: Entrapment efficiencies of Tamoxifen nanosponges.

Table 14: Entrapment efficiencies of Tamoxifen nanosponges.

S. No	Formulation code	Entrapment Efficiency (%)
1.	F1	97.45
2.	F2	93.20
3.	F3	91.89
4.	F4	96.43
5.	F5	91.72
6.	F6	97.32
7.	F7	98.61
8.	F8	93.19
9.	F9	90.35
10.	F10	88.41

The entrapment efficiency was found to be highest for F7 formulation which is 98.61 and the lowest entrapment of drug was found for F10 formulation. This might be due to the fact that the variation in entrapment efficiency was due to the changes in the polymer concentration and difference in the degree of cross linking. The prepared nanosponges possess high drug entrapment efficiency and were found to be in the range of 88.40%-98.61%.

IN VITRO DRUG RELEASE STUDIES

In vitro drug release study of the prepared. Tamoxifen nanosponges was carried out using dialysis bag diffusion method. Amount of drug released in different time intervals were observed.

In vitro drug release profile data of Tamoxifen nanosponges containing ethyl cellulose (F1- F5) are given in Table 15 and Figure 16.

Table 15: *In vitro* drug release profile of Tamoxifen nanosponges (F1-F5).

Sl. No	Time (hrs)	Cumulative percentage drug release (%)				
		F1	F2	F3	F4	F5
1	0	0	0	0	0	0
2	1	10.90	11.93	11.08	7.36	7.23
3	2	18.62	20.26	15.7	9..33	8.96
4	3	21.76	24.89	19.39	10.13	9.89
5	4	26.00	30.01	21.24	13.11	11.54
6	5	30.23	37.37	25.86	16.93	14.89
7	6	37.94	42.73	27.71	22.19	18.16
8	7	43.47	47.03	32.33	26.35	23.54
9	8	45.18	50.96	35.68	29.71	28.18
10	10	50.04	52.74	42.46	33.53	30.13
11	12	52.14	55.16	46.89	40.05	38.91
12	24	63.17	64.73	56.86	53.83	49.75
13	32	69.90	69.16	64.90	58.12	53.67
14	36	77.18	75.44	69.17	61.92	59.11
15	48	89.90	88.79	81.75	72.86	67.56

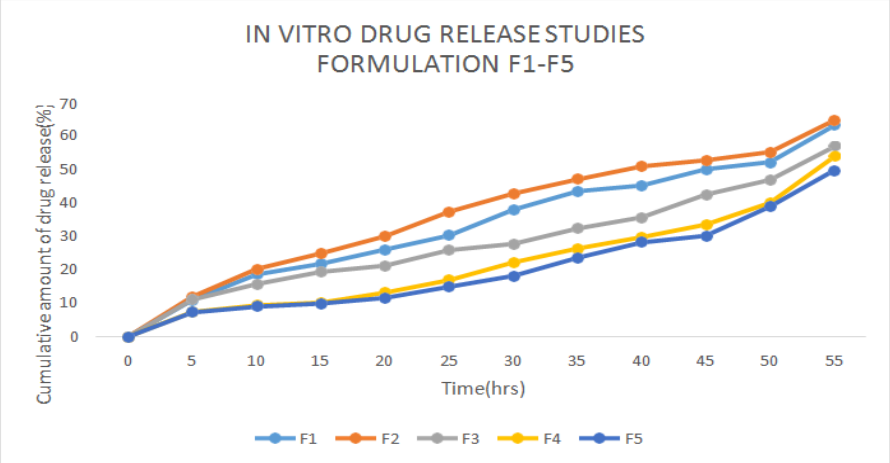


Figure 14: *In vitro* drug release profile of Tamoxifen nanosponges (F1-F5).

In vitro drug release profile data of Tamoxifen nanosponges containing eudragit (F6-F10) are given in Table 16 and Figure 15.

Table 16: In vitro drug release profile of Tamoxifen nanosponges (F6-F10).

Sl. No	Time (hrs)	Cumulative percentage drug release (%)				
		F6	F7	F8	F9	F10
1	0	0	0	0	0	0
2	1	13.44	14.32	14.06	8.99	7.45
3	2	16.48	18.35	17.77	10.27	9.06
4	3	22.39	22.14	22.26	11.30	10.87
5	4	27.18	27.04	24.41	13.10	12.12
6	5	31.4	30.05	29.05	13.87	15.68
7	6	36.16	34.24	32.02	16.44	18.86
8	7	41.64	41.08	36.57	20.55	24.98
9	8	45.19	43.61	39.09	23.76	29.12
10	10	51.4	49.35	43.43	36.99	32.19
11	12	54.16	53.67	48.13	40.18	39.16
12	24	62.41	62.53	55.89	48.91	50.80
13	32	70.85	68.51	61.24	55.16	54.89
14	36	76.18	73.27	66.75	61.19	60.23
15	48	90.18	87.10	77.94	70.14	69.86

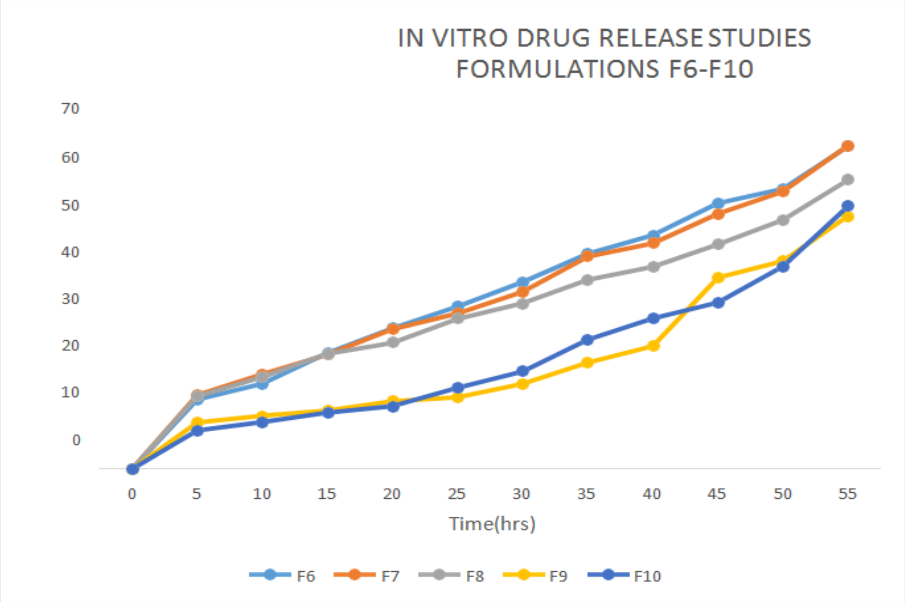


Figure 15: In vitro drug release profile of Tamoxifen nanosponges (F6-F10).

From the in vitro release data it was found that formulation F1 and F2 showed the best release of 89.90% and 88.79% respectively at the end of 48 hours among all the five formulation of Tamoxifen – ethyl cellulose nanosponges. Similarly F6 and F7 exhibited the best release of 90.19% and 87.10% respectively at the end of 48 hours amoung all the five formulations of Tamoxifen – eudragit nanosponges. The release rate was related to drug: polymer ratio. Increase of drug release was observed as a function of drug: polymer ratio. It was observed that the drug release decreased with an increase in the amount of polymer for each formulation. This may be due to the fact that the release of drug from the polymer matrix takes place after complete swelling of the polymer and as the amount of polymer in the formulation increases the time required to swell also increases. These result are in agreement with the release pattern of Tamoxifen nanoparticles observed by Hui-ping-sun et al (2016).

The newly developed nanosponges exhibit a core shell structure with a hydrophobic core formed by either ethyl cellulose (F1-F5) and eudragit (F6-F10) and a hydrophilic shell formed by PVA macromolecules. The release showed a bi-phasic pattern with an initial burst effect may due to the unentrapped drug adsorbed on the surface of the nanosponges, while remaining drug released for further few hours say around 7-8 hours may stem from drug molecule physically entrapped with in hydrophilic outer shell. At the same time, hydrophilic PVA molecules that from the shell could also solubilize within aqueous medium and release part of drug. Remaining drug is probably entrapped within the core of nanosponges and are released in the later time period.

SUMMARY AND CONCLUSION

The present work aimed at formulating Tamoxifen nanosponges with polymer name hydrophobic polymer using emulsion solvent diffusion method. This method was simple and cost effective.

Preformulation studies were carried out to find out the solubility of Tamoxifen. Solubility test gave an idea that Tamoxifen is water soluble and soluble in solvents like acetone, dichloromethane etc.

FTIR and UV spectral studies authenticate the spectra obtained with the sample drug matched with standard pure drug. UV spectra gave the maximum absorption peak at 232nm.

The comparison of FTIR spectra of Tamoxifen and mixture of Tamoxifen and polymer confirms that there is no appearance of additional new peaks and disappearance of existing peaks from that of the drug. This indicates that there is no interaction between the drug and polymer used in the study.

Formulation was carried out by emulsion solvent diffusion method. Trial batches indicated that hydrophilic polymers are not suitable for the Tamoxifen nanosponges. The hydrophilic polymers produced no yield or very less yield. Hydrophobic polymers produced good formulations. eudragit were selected for further studies.

Scanning electron micrograph of the prepared nanosponges at different magnification showed that the nanosponges were porous with a smooth surface morphology and spherical shape. The spongy and porous nature of nanosponges was clearly observed in the SEM images.

Particle size and zeta potential was determined by Malvern Zeta sizer. The particle size analysis confirmed

that the prepared sample were in the nanometer range. Average particle size obtained for the formulations F9 is 1.708e4. Zeta potential values of nanosponges indicated that the formulated nanosponges are stable.

The amount of drug being entrapped in nanosponges was calculated and all the prepared nanosponges were found to possess very high entrapment efficiency.

From the *in-vitro* release data from the dialysis bag diffusion method it was found that formulations F1 to F5 & F6 to F10 showed the best release of 89.90, 88.79, 81.75, 72.86, 67.56 and 90.18, 87.10, 77.94, 70.14, 69.86 respectively at the end of 48 hours. Increase of drug release was observed as a function of drug: polymer ratio. It was observed that the drug release decreased with an increase in the amount of polymer for each formulation. This is because the newly developed nanosponges is believed to exhibit a core shell structure with a hydrophobic core formed by eudragit and a hydrophilic shell formed by PVA macromolecules.

CONCLUSION

The Tamoxifen nanosponges can be formulated by cost effective and easy emulsion solvent diffusion method using hydrophobic polymers such as eudragit. The formulated Tamoxifen nanosponges can be used in the treatment of breast cancer. This can be targeted to the cancer cells and produce sustained drug delivery which in turn reduces the dose, frequency of administration and the side effects.

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