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RESEARCH ARTICLE
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STUDIES ON ENHANCEMENT OF ORAL BIOAVAILABITY OF PACLITAXEL BY NANO SUSPENSION TECHNOLOGY

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Abstract:
The objective of the present work was to formulate and evaluate drug release paclitaxel nano suspension for treating breast, ovarian and colon cancer effectively. Different formulations were prepared by using Solvent Evaporation technique using synthetic polymer like SLS, Edragit S 100, PVP K30, poloxamer188. The formulations were evaluated for percentage yield, entrapment efficiency, particle size analysis, and *In-vitro* drug release. The optimized formulation of the Nano suspensions containing polymer and drug was found to be compatible from FTIR studies. The *In-vitro* release of drug from the formulations were studied in pH 6.8 phosphate buffer solution, and it was found that the prepared nano suspension (F 3) were able to the drug release of the drug 45 mins of about 98.40%. and following the kinetics of first order release.

Keywords: paclitaxel nano suspension , SLS, Edragit S 100, PVP K30, poloxamer188.

Introduction: Nanotechnology opens up new vists of research in the improvement of novel drug delivery systems. “Nano” word comes from the Greek word‘ nanos ”which means dwarf [1]. Nano implies it's 10-9 or 1 billionth component. Nanosuspension is drug particle dispersion submicron colloidal. It is described in an aqueous car as dreadfully daintily colloid, biphasic, distributed strong medication droplets, size less than 1 µm stabilized by surfactants and polymers prepared by appropriate medication distribution techniques. Nanosuspension has disclosed its capacity for solving the issue of delivering drugs that are poorly water-soluble and poorly water-soluble and lipid-soluble. It improves absorption and bioavailability and helps to lower the amount of standard oral dosage forms[2,3].Micronization of inadequately soluble medicaments by colloid mills or jet mills has been chosen for a lengthy period of moment. The general distribution of particle volume varies from 0.1µm to about 25µm, with only a negligible quantity in the nanometer spectrum below 1µm.

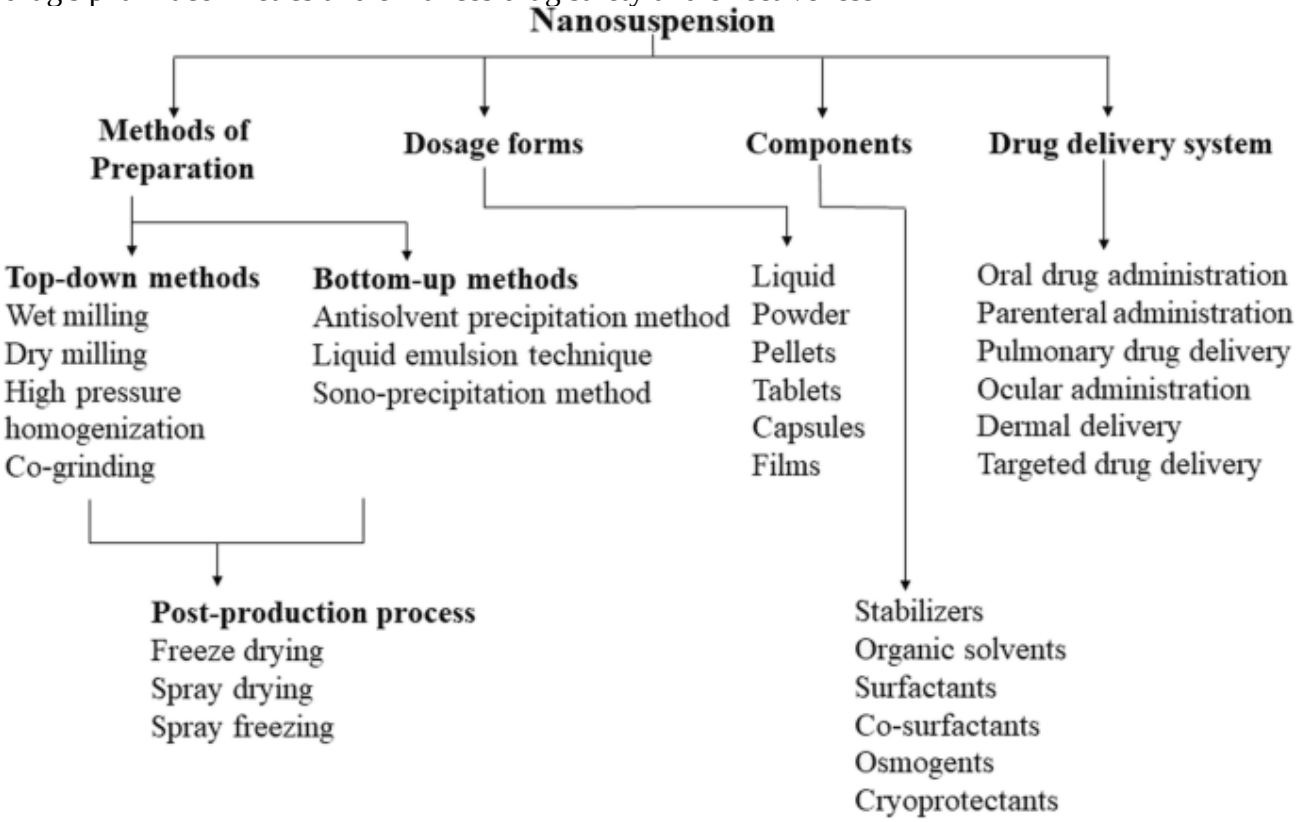
When to go for Nanosuspensions Approach

- It is intended to prepare nanosuspensions for water-insoluble compounds (but oil- soluble) with a elevated log P value.
- Usually drugs that are insoluble in water but soluble in the oil phase system are developed in

liposomes, emulsion structures, but these methods to lipid processing do not apply to all drugs.

- Nanosuspensions are favored in these instances. Nanosuspensions are used as a design strategy for drugs that are insoluble in both water and organic media instead of using lipidic structures.
- The nanosuspension design method is best suited for compounds of elevated log P value, elevated melting point and elevated dose[4,5].

Depending on the manufacturing method, modifications may happen in the drug particle's crystalline structure. An rise in the amorphous drug percentage could lead to greater solubility in saturation. Nanosuspension not only solves the issue of bad solubility and bad bioavailability, it also alters the drug's pharmacokinetics and enhances drug safety and effectiveness



Advantages:

- Most price efficient.
- Useful for drugs that are not very soluble.
- More stable physically than liposomes.
- Provide manufacturing facility and scale up for manufacturing on a big scale.
- Rapid targeted dissolution and tissue.
- Reduction of inflammation of the tissue.
- Higher bioavailability in drug delivery in the eyes and inhalation.

Potential Benefits of Nanosuspension Technology for Poorly Soluble Drugs

- Reduced particle size, enhanced medication dissolution frequency, enhanced intake frequency and magnitude, enhanced medication bioavailability, plasma vs. time curve, start-up moment, medication maximum, decreased variation, decreased fed / fasted results.
- For compounds that are water-insoluble but soluble in oil, nanosuspensions can be used. In comparison to lipidic structures, on the other side, nanosuspensions can be used to formulate compounds that are insoluble in both water and oils.
- Nanoparticles may attach to the mucosa of the gastrointestinal tract, prolonging the drug's contact period and thereby increasing its absorption.
- A significant benefit of nanosuspension is that there are many paths of nanosuspensio n administration, such as oral, parenteral, respiratory, dermal and ocular.

- Nano-suspension of nanoparticles (NPs) provides numerous benefits over standard ocular dosage forms, including decrease of dose levels, retention of drug discharge over an extended period of moment, decrease of internal toxicity of the drug, increased drug absorption owing to shorter residence time of nanoparticles on the corneal surface, greater levels of drugs in the affected tissue,
- Nanosuspension has small prevalence of exceptional side impacts.
- Nanosuspensions solve compound shipping problems by avoiding the need to dissolve compounds and by keeping the drug in a desired crystalline state of sufficient size for pharmaceutical acceptance.
- Increased hydrolysis and oxidation resistance, enhanced resting physical strength.
- Reduced amounts of administration; vital for intramuscular, subcutaneous and ophthalmic use.
- Finally, Nanosuspensions can provide the passive targeting[6,7].

METHODS OF PREPARATION OF NANOSUSPENSION

Mainly there are two methods for preparation of Nanosuspensions. The conventional methods of precipitation (Hydrosols) are called 'Bottom up technology'. The 'Top Down Technologies' are the disintegration methods and are preferred over the precipitation methods. The 'Top Down Technologies' include Media Milling (Nanocrystals), High Pressure Homogenization in water (Dissocubes), High Pressure Homogenization in non aqueous media (Nanopure) and combination of Precipitation and High-Pressure Homogenization (Nanoedege).

1) Bottom-up technology
2) Top-down technology

Bottom-Up Technology

The term "Bottom-up technology" means that one starts from the molecular level, and goes via molecular association to the formation of a solid particle.That means that we are discussing classical precipitation techniques by reducing the solvent quality, for example, by pouring the solvent into a nonsolvent or changing the temperature or a combination of both. Precipitation is a classical technique in pharmaceutical chemistry and technology.

Advantage

1) Use of simple and low cost equipment.
2) Higher saturation solubility is the advantage for precipitation compared to other methods of Nanosuspension preparation.

Disadvantages

1) The drug needs to be soluble in at least one solvent (thus excluding all new drugs that are simultaneously poorly soluble in aqueous and in organic media).
2) The solvent needs to be miscible with at least one nonsolvent.
3) Solvent residues need to be removed, thus increasing production costs.
4) It is an Iittle bit tricky to preserve the particle character (i.e. size, especially the amorphous fraction). In general, it is recommended that a second consecutive process has to be performed for particle preservation that is spray drying or lyophilization.

Top-Down Technology

The top down technologies include

a) Media milling
b) High pressure homogenization

Media Milling

Nanosuspensions are produced by using high-shear media mills or pearl mills. The mill consists of a milling chamber, milling shaft and a recirculation chamber. An aqueous suspension of the drug is then fed into the mill containing small grinding balls/pearls. As these balls rotate at a very high shear rate under controlled temperature, they fly through the grinding jar interior and impact against the sample

on the opposite grinding jar wall. The combined forces of friction and impact produce a high degree of particle size reduction. The milling media or balls are made of ceramic-sintered aluminium oxide or zirconium oxide or highly cross-linked polystyrene resin with high abrasion resistance. Planetary ball mills (PM100 and PM200; Retsch GmbH and Co., KG, Haan, Germany) is one example of an equipment that can be used to achieve a grind size below 0.1 μm. A Nanosuspension of Zn-Insulin with a mean particle size of 150 nm was prepared using the wet milling technique. The major drawbacks of this technology include the erosion of balls/pearls that can leave residues as contaminants in the final product, degradation of the thermolabile drugs due to heat generated during the process and presence of relatively high proportions of particles ≥5 μm.[20-22]

Advantages
¬ Simple technology
¬ Low-cost process regarding the milling itself
¬ Large-scale production possible to some extent (batch process).

Disadvantages
¬ Potential erosion from the milling material leading to product contamination.
¬ Duration of the process not being very production friendly.
¬ Potential growth of germs in the water phase when milling for a long time.
¬ Time and costs associated with the separation procedure of the milling material from the drug nanoparticle suspension, especially when producing parenteral sterile products.

High Pressure Homogenization
Dissocubes Homogenization involves the forcing of the suspension under pressure through a valve having a narrow aperture. Dissocubes was developed by Muller *et al.* in 1999. In this case, the suspension of the drug is made to pass through a small orifice that result in a reduction of the static pressure below the boiling pressure of water, which leads to boiling of water and formation of gas bubbles. When the suspension leaves the gap and normal air pressure is reached again, the bubbles implode and the surrounding part containing the drug particles rushes to the center and in the process colloids, causing a reduction in the particle size. Most of the cases require multiple passes or cycles through the homogenizer, which depends on the hardness of drug, the desired mean particle size and the required homogeneity. This principle is employed in the APV Gaulin Micron LAB 40 Homogenizer (APV Homogenizer, Lóbeck, Germany) and the NS 1001L-Panda 2K high-pressure homogenizer (Nirosuavi. S.P.A., Parma, Italy).[7,8]

To produce a Nanosuspension with a higher concentration of solids, it is preferred to start homogenization with very fine drug particles, which can be accomplished by pre-milling. The major advantage of high- pressure homogenization over media milling is that it can be used for both diluted as well as concentrated suspensions and also allows aseptic production.[9]

Nanopure
Nanopure is suspensions homogenized in water-free media or water mixtures. In the Dissocubes technology, the cavitation is the determining factor of the process. But, in contrast to water, oils and oily fatty acids have very low vapour pressure and a high boiling point. Hence, the drop of static pressure will not be sufficient enough to initiate cavitation. Patents covering disintegration of polymeric material by high- pressure homogenization mention that higher temperatures of about 800C promoted disintegration, which cannot be used for thermolabile compounds. In nanopure technology, the drug suspensions in the non- aqueous media were homogenized at 00C or even below the freezing point and hence are called "deep-freeze" homogenization. The results obtained were comparable to Dissocubes and hence can be used effectively for thermolabile substances at milder conditions [10,11]

Nanoedge

The basic principles of Nanoedge are the same as that of precipitation and homogenization. A combination of these techniques results in smaller particle size and better stability in a shorter time. The major drawback of the precipitation technique, such as crystal growth and long term stability, can be resolved using the Nanoedge technology. In this technique, the precipitated suspension is further homogenized; leading to reduction in particle size and avoiding crystal growth. Precipitation is performed in water using water-miscible solvents such as methanol, ethanol and isopropanol. It is desirable to remove those solvents completely, although they can be tolerated to a certain extent in the formulation. For an effective production of Nanosuspensions using the Nanoedge technology, an evaporation step can be included to provide a solvent-free modified starting material followed by high-pressure homogenization.

Emulsion Diffusion Method

Apart from the use of emulsion as drug delivering vehicle they can also be used as templates to produce Nanosuspension. The use of emulsions as templates is applicable for those drugs that are soluble in either volatile organic solvent or partially water-miscile solvent. Such solvents can be used as the dispersed phase of the emulsion. An organic solvent or mixture of solvents loaded with the drug is dispersed in the aqueous phase containing suitable surfactants with stirring to form an emulsion. The obtained emulsion was further homogenized by high pressure homogenization. After homogenization cycles the emulsion was diluted with
water, homogenized by homogenizer to diffuse the organic solvent and convert the droplets into solid particles. Since one particle is formed in each emulsion droplet, it is possible to control the particle size of the Nanosuspension by controlling the size of the emulsion optimizing the surfactant composition increases the intake of organic phase and ultimately the drug loading in the emulsion. Originally methanol, ethanol, ethyl acetate chloroform are used as a organic solvents.

Advantages

¬ Use of specialized equipment is not necessary.
¬ Particle size can easily be controlled by controlling the size of the emulsion droplet.
¬ Ease of scale-up if formulation is optimized properly.

Disadvantages

¬ Drugs that are poorly soluble in both aqueous and organic media cannot be formulated by this technique.
¬ Safety concerns because of the use of hazardous solvents in the process.
¬ Need for diultrafiltration for purification of the drug Nanosuspension, which may render the process costly.
¬ High amount of surfactant/stabilizer is required as compared to the production techniques described earlier.

Melt emulsification method

In this method drug is dispersed in the aqueous solution of stabilizer and heated above the melting point of the drug and homogenized to give an emulsion. During this process, the sample holder was enwrapped with a heating tape fitted with temperature controller and the temperature of emulsion was maintained above the melting point of the drug. The emulsion was then cooled down either slowly to room temperature or on an icebath.

Advantage

Melt emulsification technique relative to the solvent diffusion method is total avoidance of organic solvents during the production process.

Wet milling

Nanosuspensions are produced by using high shear media mills or pearl mills. The mill consists of a milling chamber, milling shaft and a recirculation chamber. An aqueous suspension of the drug is then fed into the mill containing small grinding balls/pearls. As these balls rotate at a very high shear rate under controlled temperature, they fly through the grinding jar interior and impact against the sample on the opposite grinding jar wall. The combined forces of friction and impact produce a high degree of particle size reduction. The milling media or balls are made of ceramic-sintered aluminium oxide or zirconium oxide or highly cross-linked polystyrene resin with high abrasion resistance. Planetary ball mills (PM100 and PM200; Retsch GmbH and Co., KG, Haan, Germany) is one example of an equipment that can be used to achieve a grind size below 0.1 μm. A nanosuspension of Zn-Insulin with a mean particle size of 150 nm was prepared using the wet milling technique. The major drawbacks of this technology include the erosion of balls/pearls that can leave residues as contaminants in the final product, degradation of the thermolabile drugs due to heat generated during the process and presence of relatively high proportions of particles ≥5 μm.

Hydrosol method

This is similar to the emulsification- solvent evaporation method. The only difference between the two methods is that the drug solvent is miscible with the drug anti-solvent. Higher shear force prevents crystal growth and Ostwald ripening and ensures that the precipitates remain smaller in size.[16]

Nanojet-technology

This technique, called opposite stream or nanojet technology, uses a chamber where a stream of suspension is divided into two or more parts, which colloid with each other at high pressure. The high shear force produced during the process results in particle size reduction. Equipment using this principle includes the M110L and M110S microfluidizers (Microfluidics). Dearn prepared nanosuspensions of atovaquone using the microfluidization process. The major disadvantage of this technique is the high number of passes through the microfluidizer and that the product obtained contains a relatively larger fraction of microparticles

Emulsification-solvent evaporation technique

This technique involves preparing a solution of drug followed by its emulsification in another liquid that is a non-solvent for the drug. Evaporation of the solvent leads to precipitation of the drug. Crystal growth and particle aggregation can be controlled by creating high shear forces using a high-speed stirrer.

Method of Preparation of Nanosuspension: Solvent evaporation method:

At room temperature (organic phase), Paclitaxel was dissolved in methanol. It was poured into water with various PVP K30 stabilizer,Edradit s 100, Polaxomer 188 and SLS, which was maintain at room warmth and then stirred in magnetic stirrer, stirred for thirty minutes at rpm 800-1000, to evaporate the volatile solvent. A syringe placed directly into a stabilizer containing water is used to add organic solvents. Organic solvents evaporated at a 1 hour room temperature and then Paclitaxel Nanosuspensions were formed

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Paclitaxel	320	320	320	320	320	320	320	320	320
SLS (mg)	50	100	150	--	--	--	--	--	--
Edragit S 100				50	100	150			
PVP K30 (mg)	150	150	150	150	150	150	150	150	150
Polaxomer 188	--	--	--	--	--	--	50	100	150
Methanol (ml)	5	5	5	5	5	5	5	5	5

Water (ml)	40	40	40	40	40	40	40	40	40

Evaluation parameters of Nanosuspension Paclitaxel:[12,13]

Entrapment efficacy: A cool ultra centrifugal system centrifuged the recently equipped nanosuspension at 20k rpm for 20 min at 5 ° C temperature. The amount of unincorporated medication was determined by the use of an UV spectrophotometer to control blank / nanosuspension
Absorbing the appropriately diluted 5 ml supernatant solution at 231 nm

$$\%\text{Entrapment efficiency} = \frac{\text{Drug content}}{\text{Drug added in each formulation}} * 100$$

Scanning electron microscopy: Scan electron microscopy at different magnifications show the morphology features of Paclitaxel nanosuspension.
Particle size and shape
Malvern Zetasizer ZS was used as a medium for the average particulate size and form of the formulated nanosuspension. The sample was 100 times scanned for particle size determination.
Zeta potential:
There are three ways to get a surface charge from a solid particle (colloid) scattered in a liquid medium. First of all, the ions in the solution are adsorbed. Second, by the ionization of functional groups on the particle's surface. Third, due to the difference in dielectric constant between the particle and the medium. Attention should be paid to the formation of electric double layer at the solid-liquid interface. The zeta Potential is characterized as the distinction in potential between the outside of the firmly bound layer (shear plane) and the electro-impartial district of the arrangement. The potential step by step diminishes as the good ways from the surface increments.

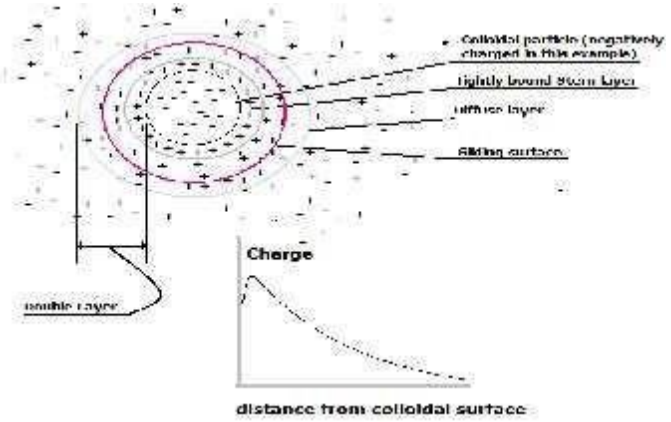


Figure : Schematic of the formation of electric double layer.

The zeta potential falls quickly as the electrolyte concentration increases in the medium due to the counter-ion screening effect (Figure). However, it can be computed with theoretical models and experimentally determined electrophoretic movement data. The zeta potential can not be measured directly. The theory is based on electrophoresis and can be expressed as:
$\mu = \zeta\varepsilon/\eta$
Where (μ) is the electrophoretic mobility, (ε) is the electric permittivity of the liquid, (η) Is the viscosity and (ζ) us the zeta potential.

Table: Zeta potential for colloids in water and their stability

Zeta Potential [mV]	Stability behaviour of the colloid
0 to ±5	Rapid coagulationor flocculation
from ±10 to ±30	Incipient instability

from ±30 to ±40	Moderate stability
from ±40 to ±60	Good stability
more than ±61	Excellent stability

***In-vitro* drug release study:**

Using the 900 ml 6.8pH tampon as a dissolution means maintained at 37±0.5 ° C and rattling speed (50 rpm), USP dissolution apparatus-type II was conducted with the in vitro dissolution study. Nanosuspension were supplemented to the dissolution medium, five- milliliter samples were withdrawn at specific intervals of time, then clean through a 0.45 µm filter paper and analyzed for their drug concentrations by measuring at 231 nm wavelength.

The results of in vitro release profiles obtained for the formulations were fitted into two models of data treatment as follows:[14,15]

1. %CDR versus time (zero order kinetic model).
2. Log %ARA versus time (first- order kinetic model).

Table no ; Drug release kinetics

Kinetic Model	Relation	Systems Following the Model
First order	$\ln Q_t = \ln Q_o + Kt$ release is proportional to amount of drug remaining	Water-soluble drugs in porous matrix
Zero order	$f_t = K_o t$ (independent of drug concentration)	Transdermal systems Osmotic systems

RESULTS AND DISCUSSION

Determination of melting point

Paclitaxel melting point was determined to be 212ºC by capillary method.Saturation solubility was carried out at 25^0C using 0.1N HCL, 6.8 phosphate buffer, and other solvents.

Media	Solubility(mg/ml
0.1N HCL	0.568
Ethanol	0.985
Methanol	1.263
pH 6.8 phosphate buffer	0.923
pH 7.4 phosphate buffer	0.754

Discussion: From the above solubility studies conformed that pH 6.8 phosphate buffer has greater solubility when compared with other buffers and methanol shows greater solubility than ethanol.

Determination of absorption maximum (λmax):

Paclitaxel λ_{max} was determined for precise quantitative estimation of the dissolution tempo at pH 6.8 buffer medium.

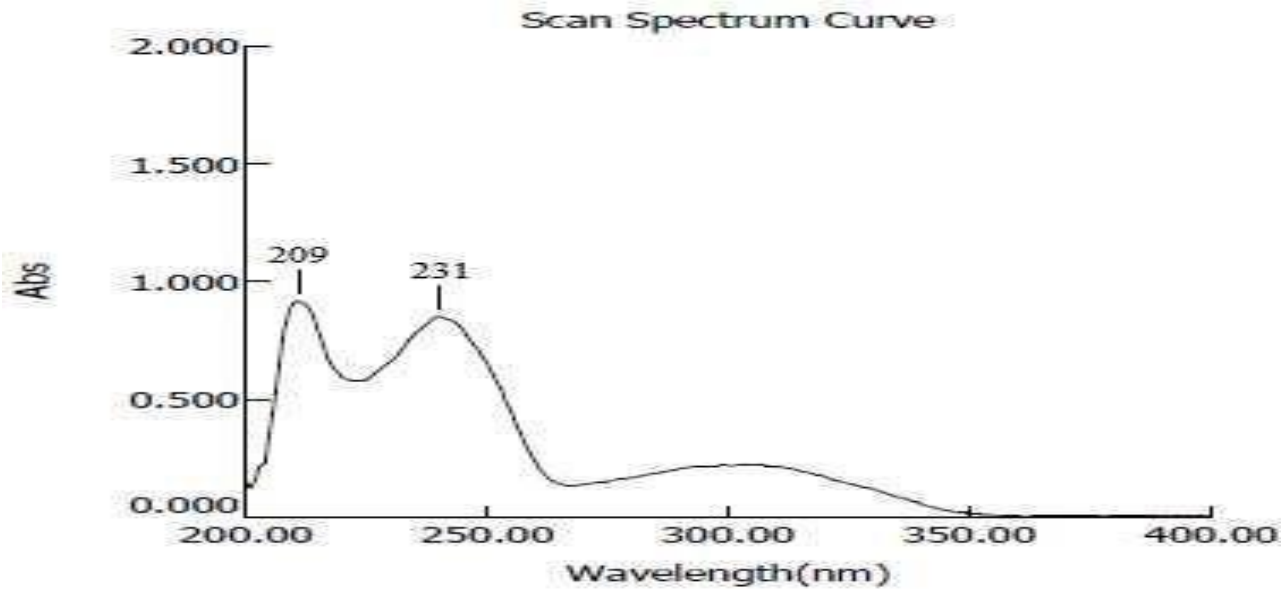
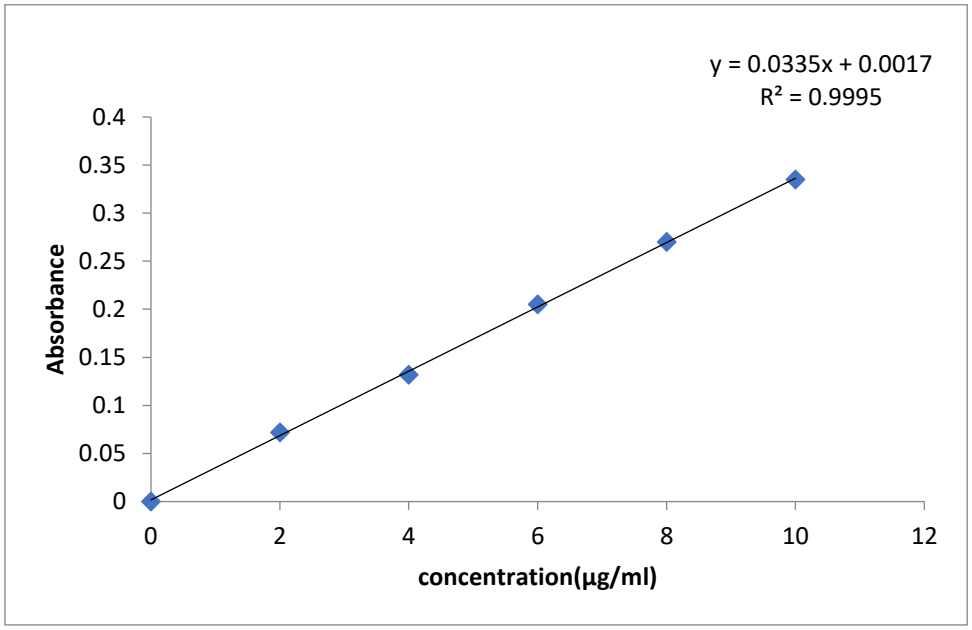


Fig: Uv Spectrum of Paclitaxel

Calibration curve values for estimation paclitaxel in 6.8 pH phosphate buffer:
Standard calibration values (Absorbance values) of paclitaxel:

no	Concentration (µg/ml)	Absorbance
1	2	0.072
2	4	0.132
3	6	0.205
4	8	0.270
5	10	0.334

Table: Standard graph of Paclitaxel in pH6.8 (λmax 231nm)



Drug excipient compatibility:

Figure No 4: FT-IR Reports for API (paclitaxel)

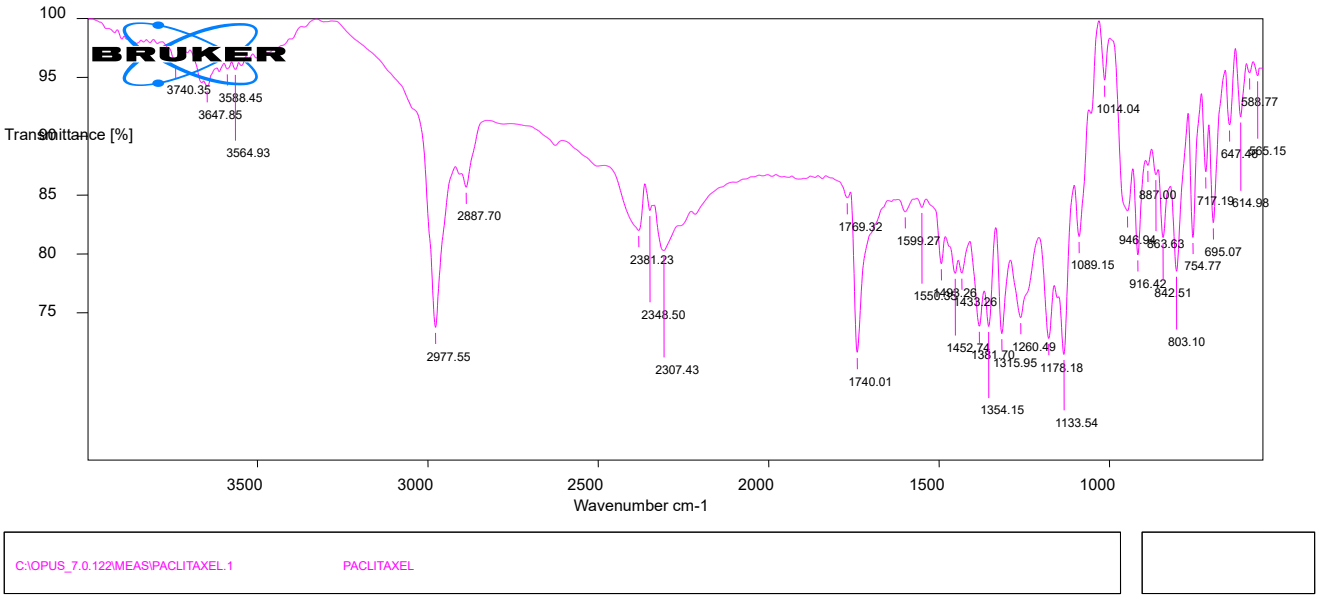


Figure: IR spectrum of Paclitaxel

Discussion: We observe forms of drug compatibility studies that no interactions exist between pure drug(Paclitaxel) and optimized formulation(Paclitaxel + excipients).

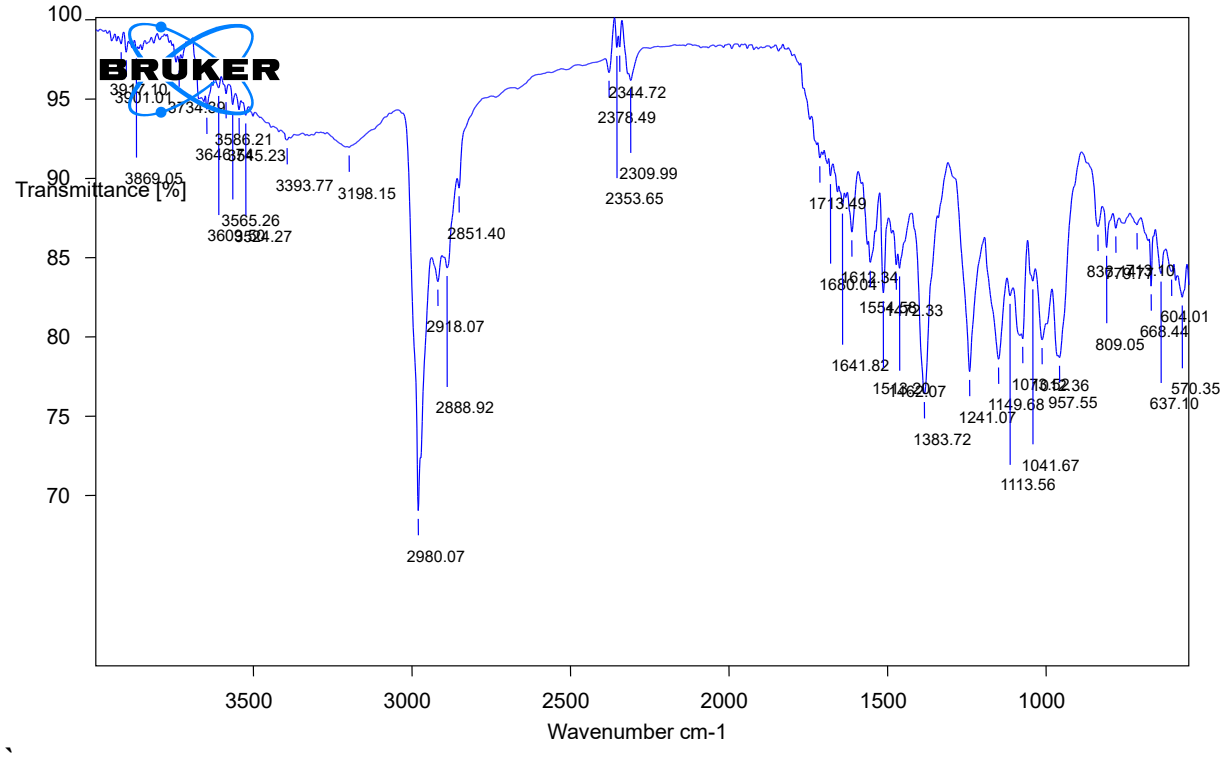


Figure: IR spectrum of Paclitaxel Optimised Formulation

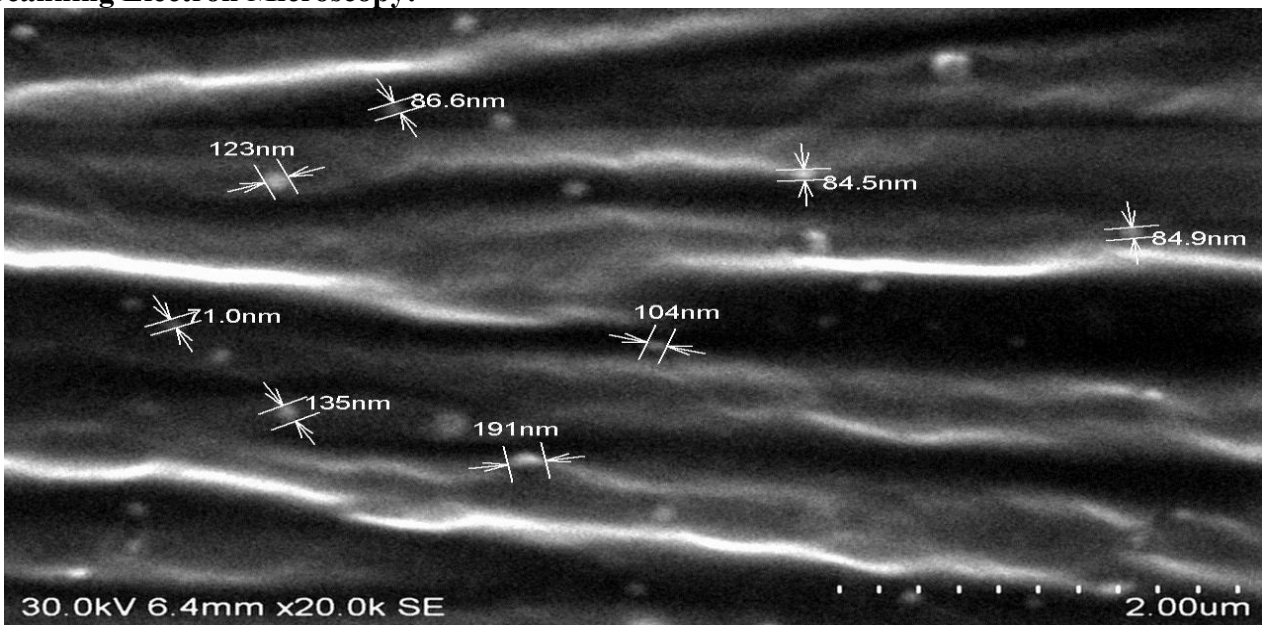
Table: Entrapment efficiency, Viscosity of formulated Nanosuspensions

Formulation code	Mean % entrapment efficiency	Viscosity (cps)
F1	86.36±0.54	42.4±2.1
F2	92.10±0.24	44.3±1.1
F3	96.54±0.52	45.3±2.1
F4	83.20±0.10	48.4±3.6

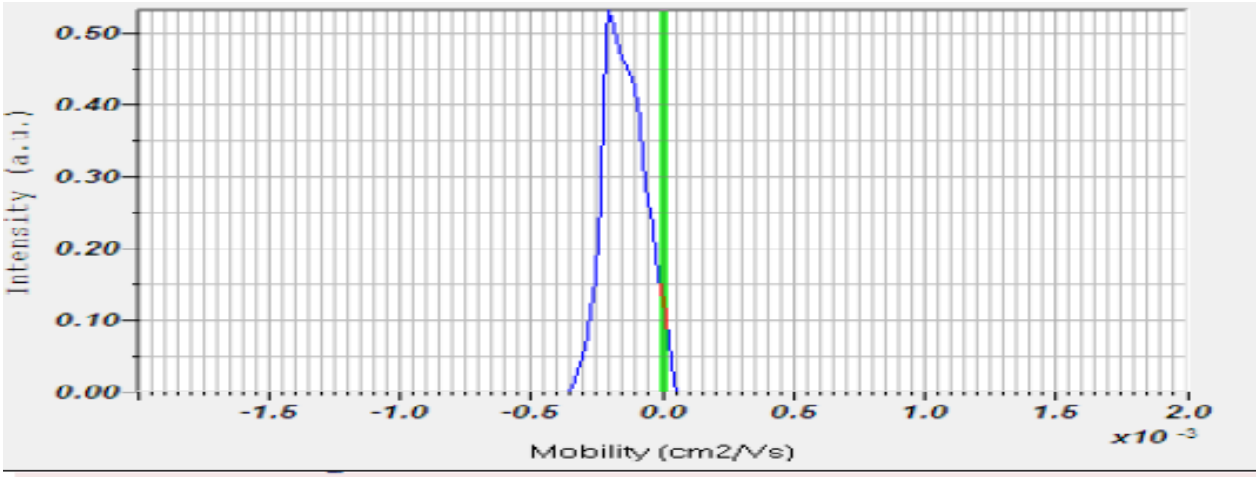
F5	90.69±0.29	47. ±2.8
F6	95.02±0.39	51.6±2.3
F7	90.22±0.52	55.3 ±2.1
F8	91.53±0.36	57.2±2.9
F9	94.22±0.49	59.3±2.2

Discussion: The entrapment efficacy of formulation F1-F9 were within 86.36±0.54%- 96.54±0.52%. The viscosity of nano suspension were with in 42.4±2.1 - 59.3±2.2

Scanning Electron Microscopy:



Zeta Potential: The measurements themselves are a fluid electrophoresis, the doppler change of laser light dispersed by motioning electrons determines the particle velocity. The field force was 20 V / cm. With the Helmholtz-Smoluchowski equation, electrophoric movement has been transformed into a zeta force in mV.



Calculation Results

Peak No.	Zeta Potential	Electrophoretic Mobility
1	-19.2 mV	-0.000149 cm2/Vs
2	--- mV	--- cm2/Vs
3	--- mV	--- cm2/Vs

Zeta Potential (Mean) : -19.2 mV

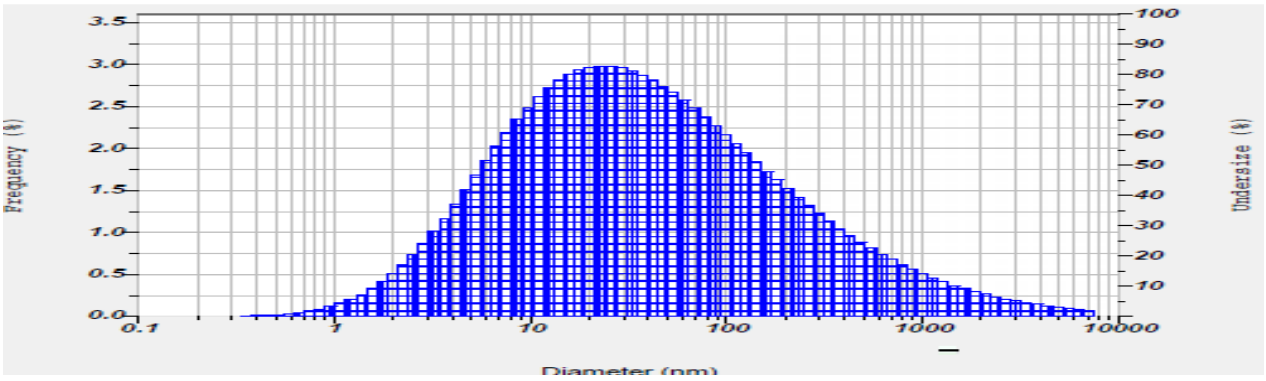
Electrophoretic Mobility Mean : -0.000149 cm^2/Vs

Discussion: Zeta potential value for the optimized formulation (F3) were within the acceptable limits.

Particle size analysis:

Peak No.	S.P.Area Ratio	Mean	S. D.	Mode
1	1.00	179.5 nm	538.2 nm	22.9 nm
2	---	--- nm	--- nm	--- nm
3	---	--- nm	--- nm	--- nm
Total	1.00	179.5 nm	538.2 nm	22.9 nm

Cumulant Operations
Z-Average : 5.6 nm
PI : 2.206
Molecular weight measurement
Molecular weight : ---
Mark-Houwink-Sakurada parameters : ---



Discussion: The average nano-suspension particle size (F3), with peak sizes of 179.5 nm, was shown to be of optimized formulation.

Dissolution results:

Table: *In-vitro* drug release data of formulation F1to F9

TIME	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0

5	23.62±0.52	36.84±0.02	43.56±0.23	41.75±0.23	30.62±0.22	22.69±0.54	32.52±0.53	39.84±0.2	30.20±0.29
10	29.52±0.41	43.51±0.34	52.41±0.40	48.52±0.45	49.63±0.12	44.21±0.61	39.84±0.26	49.61±0.13	47.85±0.96
15	35.08±0.96	57.84±0.65	63.41±0.85	59.52±0.16	56.95±0.36	50.63±0.56	46.82±0.09	57.06±0.56	59.61±0.32
20	49.12±0.32	64.85±0.98	69.85±0.54	67.52±0.33	69.85±0.63	64.29±0.42	53.74±0.14	70.33±0.91	66.75±0.63
30	60.85±0.05	76.84±0.86	76.95±0.91	81.63±0.69	78.51±0.59	74.63±0.18	69.85±0.32	79.82±0.38	74.08±0.44
45	72.63±0.54	85.63±0.43	85.41±0.62	88.63±0.93	89.63±0.45	86.41±0.64	77.05±0.60	89.63±0.62	89.63±0.01
60	80.96±0.23	92.63±0.24	98.4±0.51	92.63±0.32	97.42±0.21	92.22±0.35	86.63±0.22	92.02±0.23	98.4±0.20

Discussion: All formulations are shown in-vitro dissolution information and numbers show dissolution patterns. In vitro drug discharge information from all Paclitaxel nanosuspension formulations were exposed to fitness tests on linear regression analyzes by zero order first order kinetics and substance release equations. The findings of linear regression assessment, with regression coefficients derived from the above information, show that an optimized approach (F3).

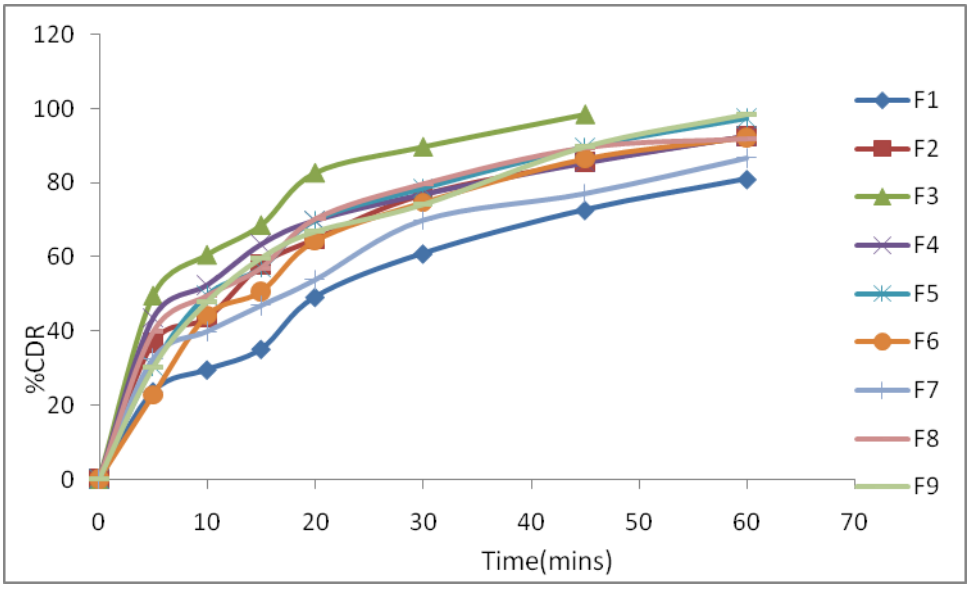


Fig Dissolution parameters for the formulations F1-F9

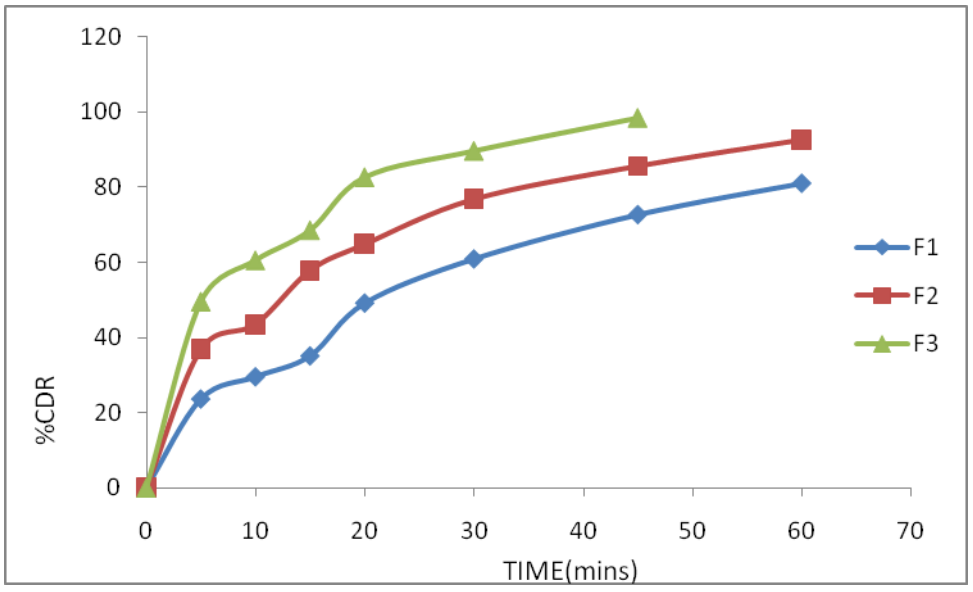


Fig Dissolution parameters for the formulations F1-F3

Discussion: FormsF1-F9 were drawn up with three different SLS (e.g. 60,120&180 mg) in formulationsF1-F3. In the above studies in in vitro we can say that at the end of 45 minutes 180 mg SLS indicates a peak drug release. So further trails were formulated to decrease the drug release time.

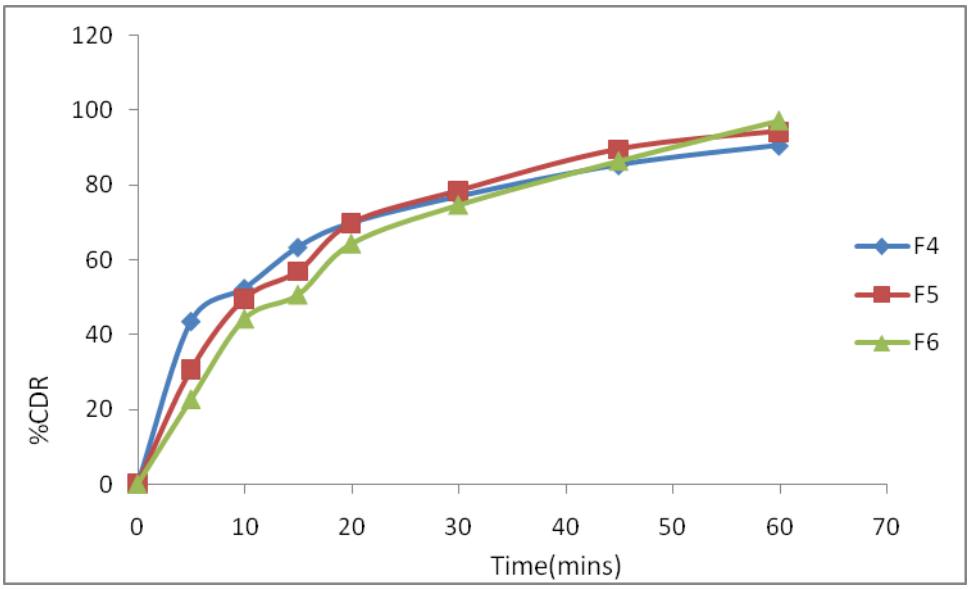


Fig Dissolution parameters for the formulations F4-F6

Discussion:

Formative formalities of F4-F6, in three ratios (e.g. 60,120&180 mg) were developed using PVPK-30. From the above invitro studies we can say that 180mg of PVPK-30 shows maximum drug release at the end of 30mins, where as remaining F4 & F5 formulatoions 45-60mints. So further trails were formulated to decrease the drug release time.

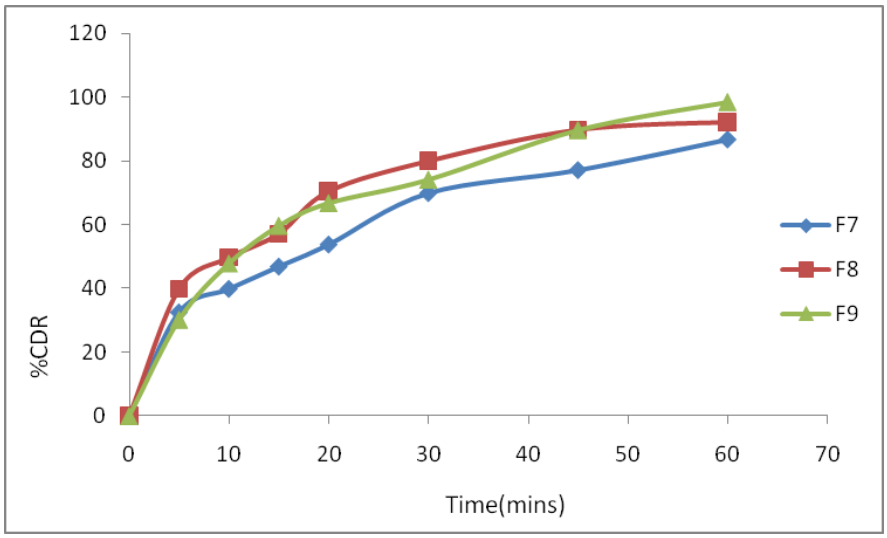


Fig Dissolution parameters for the formulations F7-F9

Discussion: The formulation of F7-F9 was formulated in three different ratios using poloxamer (i.e. 60,120&180 mg). In the above in vitro research it can be said that the peak discharge of 40 mg of the poloxamer occurs at the end of 45 minutes and the remaining formulations are F7 & F8 at 60 minutes.We can tell in the above in vitro research that the increasing amount of polymers reduces all formulations during their processing.

Thus F3 is regarded as optimal as drug discharge in 45 minutes can be seen.

Drug release kinetics studies: Best formulation F3

ZERO ORDER RELEASE KINETICS:

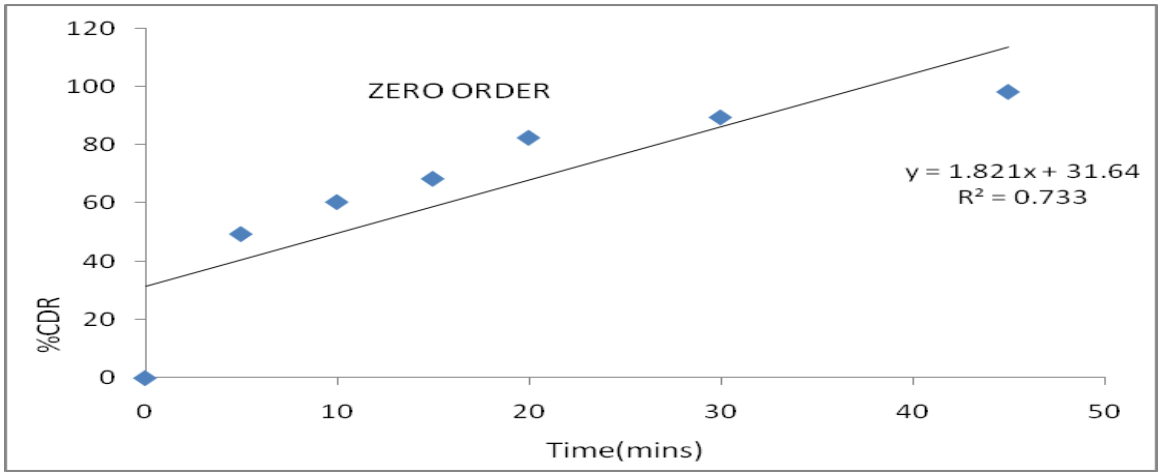


Fig: Zero order release profile of formulation F3

FIRST ORDER RELEASE KINETICS:

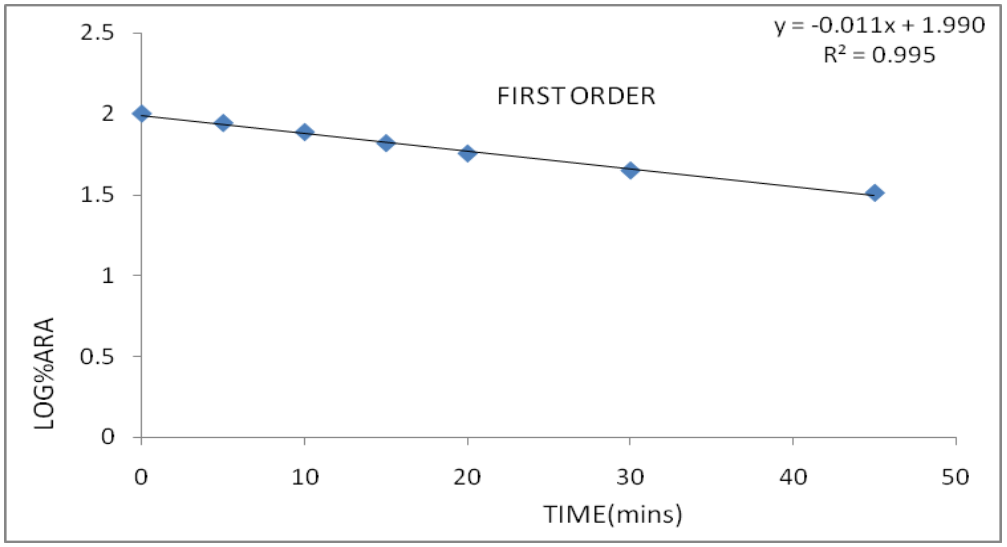


Table: Kinetic data of the formulation F3

ORDE OF KINETICS	ZERO ORDER	FIRST ORDER
REGRESSION	0.733	0.995

Discussion:

Nanosuspension drug release was clarified by the use, first order, of mathematical model equations as zero order. Based on the regression scores, the optimized model F3 has been found with kinetics of first order.

SUMMARY

Paclitaxel is used to treat ovarian cancer. By enhancing its dissolution, the effectiveness of Paclitaxel can be improved. Reducing the particle size to nanoscale can assist the surface area boost to improve formation. It can be developed as a nanosuspension because of its elevated half-life. Nanosuspension is a novel method used to progress drug solubility by solvent evaporation. The Nano suspensions represent a new, promising target and controlled dosage form, important for the easy production and diversified applications. The current tendency is that biodegradable polymer is used because of its accessibility and low toxicity in pharmaceutical research. The technique of solvent evaporation using SLS, Polaxomer, Edragit s 100, PVP K30 and methanol was worn to produce the drug-containing nanosuspension as organic solvents.

In this study the solvent evaporation technique is worn to develope nanosuspension.

The Nano suspensions are a successful new destination and regulated released dosage, which is increasingly important due to the ease of production and the wide range of apps. The current trend in pharmaceutical research is the use, thanks to its accessibility and small toxicity, of biodegradenable polymer.

Drug-containing nanosuspension has been formulated using a technique of solvent development using SLS, Polaxomer, Edragit s 100.PVP-K30, and methanol mixes and adequate water quantities. Spectrophotometrically at 231 nm, an estimate of Paclitaxel was carried out.

For parameters such as entrapement effectiveness, electron scanning, particle size testing, in-vitro discharge possibilities, interactions between drug excipients (FTIR), Nanosuspension was assessed. The MP of Paclitaxel was determined by capillary technique in the assortment of 212 ° C.

Saturation solubility with 0.1N HCL, 6.8 phosphate and organic solvents was performed with 250C. Form the drug excipient compatibility studies we observe that there are no interactions between the pure drug (Paclitaxel) and optimized formulation (Paclitaxel+ excipients) which indicates there are no physical changes.

The trapping effectiveness was discovered to be 86.36±0.54%- 96.54±0.52% respectively, of the designed Nanosuspension.

The zeta value was discovered to be within reasonable boundaries of the optimized formulation (F3). The average particle size of the optimized formulations nanosuspension (F3) was 179.5nm.

The in vitro research indicate that F3 is the finest method to deliver 98.40 percent of the medications within 45 minutes when all other formulations need 45-60 minutes to discharge the medicine. The release of the medication from the Nanosuspension was clarified by the first order of first order, by mathematical model equations. Due to regression scores the optimized formula F3 has been found following kinetics of the first order

CONCLUSION

From the present study, the following conclusions can be drawn:

- Oral Nanosuspension of Paclitaxel using multiple polymers such as SLS, Polaxomer, Edragit S 100,PVP-K30 and Methanol through a solvent evaporation technique.
- The entraoment efficiency was shown to be 86.36±0.54%- 96.54±0.52% respectively of the designed nanosuspension.
- As the polymer concentration increases, the drug release time decreases, whereas Nanosuspension strength increases.
- The first-order release kinetics and pre-discharge were exhibited with optimized nanosuspension formulations.
- IR-spectroscopic surveys show that there is no interactions within drug & its exceipients.
- The Optimized formula is compared to all other F3 formulations indicates that 98.402 per cent of drugs with first-order releases were published within 45 minutes.

The study concluded that Paclitaxel drug solubility was successfully increased by using Nanosuspension prepared using SLS (180 mg) solvent evaporation technique

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