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Bioavailability Enhancement of BCS Class IV Drug Docetaxel Using Mesoporous Silica Loaded Phospholipid Complex

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ABSTRACT

The Solid dispersion of Mesoporous silica loaded phospholipid complex for Docetaxel a BCS class IV drug was prepared by Solvent evaporation methodto improve the oral bioavailability of the model drug Docetaxel and the cellular uptake i.e. permeability study was investigated. The drug Docetaxel is a plant alkaloid effective in the treatment of metastatic breast cancer with a first line chemotherapy regimen but it is only available in market as Intravenous infusions as oral bioavailability of Docetaxel is only 8%±6%. According to the Solubility studyand in-vitro dissolution study, the results demonstrated an improved solubility of Docetaxel by using phospholipid and mesoporous silica nanoparticle as drug carriers compared to free docetaxel. The evaluation on Everted sac technique revealed that Drug PC-SD exhibit a significant increase in the absorptive permeability.

The results indicated that MSN and phospholipid could be very potential drug delivery carriers for poorly bioavailable or for hydrophobic drugs.

KEYWORDS: Solid dispersion, Mesoporous silica, Phospholipid complex, Solvent evaporation method, Permeability.

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INTRODUCTION [1,2]

The current major challenges in pharmaceutical industry are generally related to the strategies that improves solubility and permeability of the drugs. So there are number of studies which are performed with the aim to increase solubility, dissolution rate and permeability of the Class II and IV drugs.

As plant derived drugs have gained increasing popularity to the medicine markets as safer and effective substitutes of new synthetic medicines which are to be considered as adverse and toxic interactions. The results of this drug are satisfying the primary healthcare needs of population of 65-80% in developing or developed nations. However, the bioavailability of active plants derived has become an issue of concern for researchers because of poor oral bioavailability.

According to the Bio pharmaceutics classification system (BCS), class IV drugs show most challenging molecular properties with both low aqueous solubility and poor membrane permeability. To contradict these problems, there are many novel drug delivery systems developed in the recent time, including liposomes, nanoparticles, complexation with cyclodextrins, self-microemulsifying drug delivery and lipid emulsion. However, the lower drug-loading capacity and encapsulation efficiency allied with the large amount of surfactant or absorption enhancer make these way unsuitable to deliver sufficiently high clinical doses of BCS IV class drug.

In recent years, the proficiency of complexing drugs with phospholipids has appeared as a challenging but fortunate method for improving the bioavailability and therapeutic efficacy of a number of poorly absorbed drugs. Compared with other methods, this technique is comparably simple and safe. It include phospholipid molecules containing phosphatidylcholine into complex with standardized herbal extracts and/or specific active pharmaceutical ingredients to improve the n-octanol/water partition coefficient (lgPo/w), membrane permeability and, hence, the systemic bioavailability of these drugs. Although Phospholipid Complex may notably increase membrane transport, its property of high viscosity and poor water-solubility makes the complex drug dispersion and dissolution rate low in aqueous media, including gastrointestinal fluid, which precede to negative consequence on absorption

Recently, mesoporous silica- based solid dispersion (SD) has acknowledged increased attention. Large surface area and pore volume make mesoporous silica materials magnificent candidates for proficient drug loading and rapid release. Among mesoporous silica materials, SBA-15 (Santa Barbara Amorphous-15) and MCM-48 (Mobil Composition of Matter-48) are common representatives of mesoporous silica materials applied as drug carriers. The concept of combined drug delivery system

(CDDS) in which two different drug delivery systems are merged together to conquer drawbacks of traditional delivery systems has been put forward since the beginning of this century. For example, CDDS composed of solid dispersion not only increases oral bioavailability of the loaded drugs, but also controls their release rates.

Now, several approaches for improving drug delivery, solubility and permeability are constantly designed and modified, specifically for class II and IV compounds. The approaches such as complexation, micronization, crystal modification, increasing the drug dissolution rate, higher solubilization of the drugs etc., are more explored but these techniques do have restrictions to improve the assimilation and permeability of class IV drugs. Consequently, the best solution to improve the bioavailability of these drugs would be to return to the lead optimization phase of drug discovery and alter their structures to obtain the appropriate physicochemical properties. Biopharmaceutics classification system (BCS) class IV compounds, exhibits least oral bioavailability, low solubility and intestinal permeability among all pharmaceutical classes of drugs. Thus, these drugs need more compatible and efficient delivery system. Since, their solubility in various medium remains a limitation.

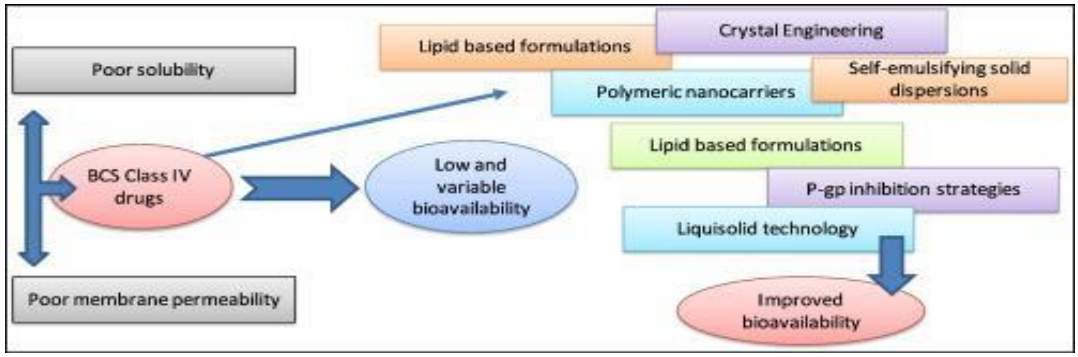

Fig. no. 1 scheme for improving the solubility and permeability of BCS class IV drug

The pharmaceutical drugs formulated for systemic delivery via the oral route of administration are irrespective of the mode of delivery (immediate, sustained or controlled release) and the design of dosage forms (either solid dispersion or liquid) must be developed within the intrinsic characteristics of gastrointestinal physiology, pharmacokinetics and pharmacodynamics as formulation design is essential to achieve a systemic approach to the successful development of an oral dosage form. Solid oral delivery system is system of choice among all drug delivery system and they do not require special treatment/ and are therefore less expensive to manufacture.

Therefore, most of the new chemical entities underdevelopment these days are purposefully used as a solid dosage form which produces an effective reproducible in vivo plasma concentration after oral administration. In fact, most new chemical entities are poorly soluble drugs, not well-absorbed after oral administration, which can amuse from the drug's essential efficacy. Drug absorption from the gastrointestinal tract can be bounded by a number of factors; most consequential contributors are poor aqueous solubility & poor membrane permeability of the drug molecule. When delivering an active agent orally, it must first dissolve in gastric and/or intestinal fluids before it can permeate the membranes of the GI tract to reach systemic circulation. Hence two areas of pharmaceutical research that focus on improving the oral bioavailability of active agents include enhancing solubility and dissolution rate of poorly water soluble drugs & enhancing permeability of poorly water-soluble drugs.

One of the major current challenges of the pharmaceutical industry is allied to strategies that improve the water solubility of drug. Drug release is a essential and limiting step for oral drug bioavailability, especially for drug with low gastrointestinal solubility and permeability. By recuperating the drug release profile of these drugs, it is possible to enhance their bioavailability and reduce side effects.

1.2 The carrier used for nanoparticles are:

- Phospholipid
- Mesoporous silica

PHOSPHOLIPIDS:[4,5]

In general, fats, phospholipids, and steroids are various types of lipids present in the body and perform different various functions. From them, phospholipids are major components of cell membranes which also serves as a vehicle, thus making the design of drug delivery systems more flexible, and are suitable for the body needs. Phospholipids are bio friendly and offer various benefits such as formulation flexibility and the choice of different NDDS based on the intended use. Phospholipids are lipids which contains phosphorus, a polar portion and non-polar portion in their structures.

A human biological membrane contains different classes of phospholipids, like phosphatidy lethanolamine (PE), phosphate idylinositol (PI), phosphatidyl choline (PC), phosphatidic acid (PA), and phosphatidyl serine (PS). PC contains two neutral tail groups and a positive head group which contains an oxygen atom in the phosphate group that has a strong tendency to gain electrons, while

nitrogen to lose electrons, a rare molecular characteristic that makes PC miscible in both water and lipid environments.

Earlier "Lecithin" is a word which made perplexity in researchers for identification but later on it was clearly discussed by Wendel. In commercial perspective, lecithin relates to PC, PE, PS, PI and other phospholipids. But in historical point of view lecithin includes lipids which contains phosphorous which are obtained from brain and egg. However, scientifically lecithin refers to Phosphotidylcholine (PC).

Phospholipid complexes are absorbed from the GIT through enterocyte based transport, and drug transport to the systemic circulation via intestinal lymphatic system which has widespread network throughout the body. The major advantage of lymphatic transport is to bypass the first-pass metabolism and are applied for targeted drug delivery.

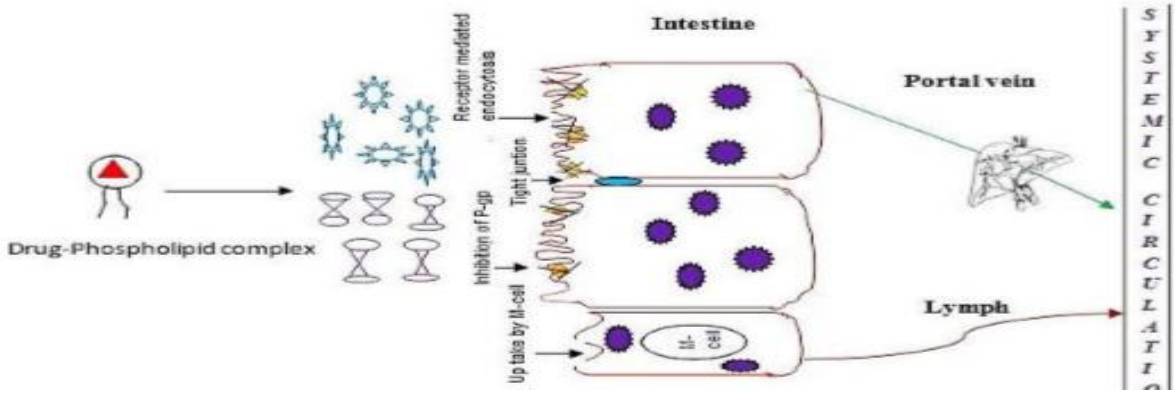

Fig. no. 2 Transport of Drug-phospholipid complex from GIT through enterocyte transport

MESOPOROUS SILICA NANOPARTICLES (MSNs) [6,7,8,9,10,11]

Mesoporous silica nanoparticles (MSNs) are occupying increasing interest for potential biomedical applications. With tailored mesoporous structure, huge surface area and pore volume, selective surface functionality, as well as morphology control, MSNs evidences high loading capacity for therapeutic agents and controlled release properties if modified with stimuli responsive groups. Recently, mesoporous silica based solid dispersion (SD) has received increase attention. Large surface area and pore volume make mesoporous silica materials excellent candidates for efficient drug loading and rapid release. Among mesoporous silica materials, SBA-15 (Santa Barbara Amorphous-15) and MCM are typical representatives of mesoporous silica materials applied as drug carriers.

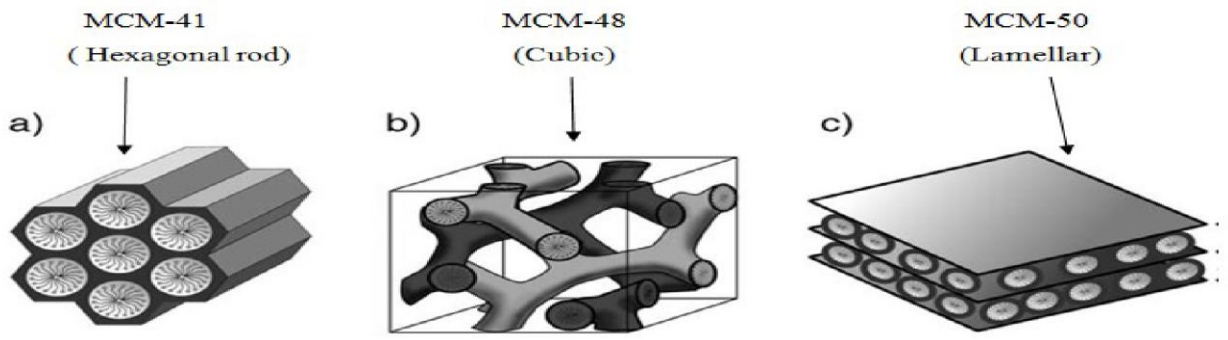

Fig. 3 Structures of mesoporousM41S materials a) MCM-41 (2D hexagonal, space group p6mm), b) MCM-48 (cubic, space group Ia3d), and c) MCM-50 (lamellar, space group p2).

MESOPOROUS SILICA-BASED SYSTEM FOR POORLY SOLUBLE DRUGS

With the increasing numbers of innovative new drugs in development, almost 70% of new drug candidates exhibit low aqueous solubility, ultimately resulting in poor absorption[9]. In an attempt to overcome this solubility obstacle and to improve the oral bioavailability, a growing number of drug delivery technologies have been developed. Presently, nanotechnology is attracting increasing attention as it can be applied in two aspects: processing the drug itself into nano-sized particles or preparing drug-contained nanoparticles from various materials. With the excellent features including huge surface area and ordered porous interior, mesoporous silica can be used as a perfect drug delivery carrier for improving the solubility of poorly water-soluble drugs and subsequently enhancing their oral bioavailability.

When water-insoluble drug molecules are contained in mesoporous silica, the spatial confinement within the mesopores can reduce the crystallization of the amorphous drug. Compared with the crystalline drug, the amorphous drug can reduce the lattice energy, subsequently resulting in improved dissolution rate and enhanced bioavailability. Moreover, the huge hydrophilic surface area of mesoporous silica facilitates the wetting and dispersion of the stored drug, resulting in fast dissolution.

SOLID DISPERSION: [12,13]

The concept of solid dispersion was originally proposed by *Sekiguchi*and *obi*.

It is defined as a method for dispersing one or more active ingredients on a water insoluble carrier of extremely high surface area to achieve increased bioavailability and dissolution rates of insoluble drugs. Solid dispersion uses the solvent deposition technique to increase the solubility, dissolution and bioavailability of many insoluble or poorly water soluble drugs. *In-vivo* results have

confirmed the fact that solid dispersion improves the release profile of many drugs resulting in rapid onset of bioavailability.

Need of Solid dispersion:

- Increases the Oral bioavailability of a drug Increases the dissolution rate.
- Enhances the release of drugs from ointment.
- Improvement in the solubility and stability.

Selection of a Carrier:

- Freely water-soluble.
- Non-toxic and pharmacologically inert.
- Soluble in various solvents.
- Chemically compatible with drugs.

MATERIAL AND METHODS:

Table no. 1 list of materials

Sr. no.	Chemicals	Manufacturers
1	Docetaxel	Merck Pharmaceutical
2	Parteck silica SLC	Merck pharmaceutical
3	Ethanol	Modern science lab
4	Disodium hydrogen phosphate	Modern science lab
5	Potassium dihydrogen phosphate.	Modern science lab
6	Conc.HCL	Modern science lab

Preparation and Optimization of Drug Pc-Sd:

STEP I: Preparation and optimization of Docetaxel-Phospholipid complex.

Table no 2: Design factor and levels for the optimization of Drug-PC:

FACTORS	LEVELS		
	1	2	3
Molar ratio of DTX to phospholipid	1:1	1:1.5	1:2

STEP II: Preparation of Docetaxel Phospholipid complex- Solid dispersion(DTXPC-SD):

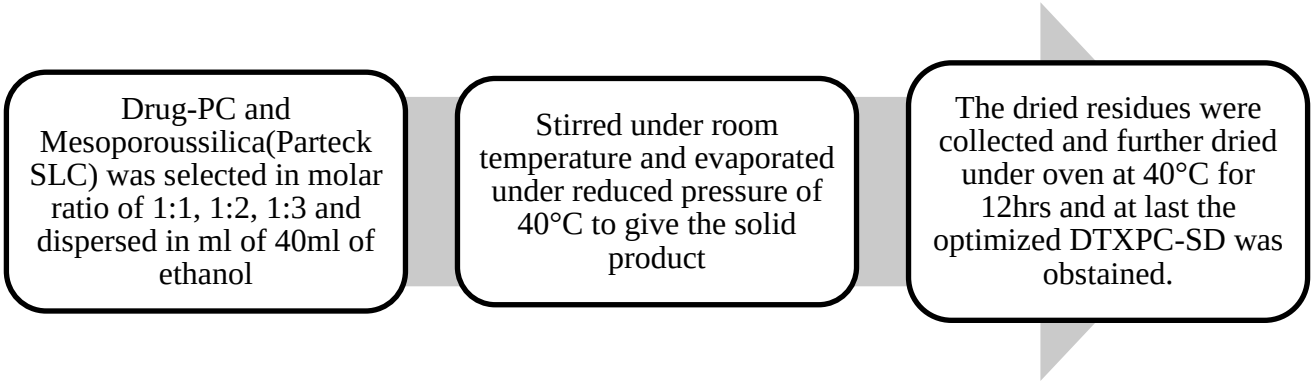

Table no 3: Design of factor and levels for the optimization of DTXPC-SD:

FACTORS	LEVELS		
	1	2	3
Molar ratio of DTX & phospholipid TO MSN	1:1	1:2	1:3

CHARACTERIZATION METHODS OF DRUG, DRUG-PC, DRUGPC-SD

ATR spectroscopy

The representative sample of Docetaxel was mixed with IR grade KBr in 1:100 ratios and was triturated to obtained uniform blend. This blend was dried for 10 min under IR lamp and then it was subjected to FT-IR (Jasco 4100) scan in the range of 400- 4000 cm-1.

Differential scanning calorimetry (DSC)

Thermal analysis of Docetaxel plain drug and drug loaded mesoporous carriers were carried out by using Mettler Toledo DSC system operating with STAR^e software. Indium was used for calibration. The sample cell was purged with dry nitrogen at a flow rate of 60 ml/min. Accurately weighed samples of 5 – 10 mg were placed in aluminum crimped pans with a pin hole and scanned at a heating rate of 10 ^{0}C/min over a temperature range of 30 – 300 ^{0}C.

Scanning electron microscopy (SEM)

SEM images of Docetaxel plain drug, mesoporous plain carrier and drug loaded mesoporous

carriers were taken from the SEM (JEOL JSM - 5600) instrument to study the morphology. The powder samples were mounted over a double sided adhesive carbon tape which were mounted over aluminum pin stubs and sputter coated with gold using ion sputter. The powder samples which were not adhered on to carbon tape were blown out gently and finally the samples were visualized under SEM instrument.

Powder X-ray diffraction analysis (PXRD)

PXRD pattern of plain drug and drug loaded carriers were recorded by using an MAXima X XRD-7000 (Shimadzu, Japan) X-ray difractometer operated at a voltage of 40 kV and current of 30 mA using Cu Kα radiation source (1.54 Å) passing through nickel filter with divergence slit (1^0), scatter slit (1^0) and receiving slit (0.3 mm) over the angular range (2θ) of 10– 40^0 at a rate of 4° min^{-1} in steps of 0.02^0 with step time of 0.3 second.

EVALUATION STUDY

Solubility study

Solubility study was conducted in different media (0.1 N HCl, 7.4 pH phosphate buffer, water, ethanol and methanol). Docetaxel powder in excess amount was added to 10ml of each media in 10ml volumetric flask and then kept for shaking in orbital shaking incubator (Lab Companion Model SI-300) at an agitation rate of 100 rpm for 48 hr at 37 ^{0}C. After the equilibration period of 48 hr the samples were removed and subjected to centrifugation (SIGMA 3K30 centrifuge) at 10,000 rpm, for 10 min at 37 ^{0}C. The supernatant was then analyzed by UV-visible spectrophotometer (V-650, Jasco, India) at 229 nm with appropriate dilutions in ethanol.

Determination of drug content

Docetaxel content in all drug loaded mesoporous silica nanoparticles were determined by taking weighed quantity of DTX-MSN i.e. 200mg in 10 ml ethanol. Then sonicated (CITIZEN LAB CD 4820.) for 10 min. Concentration of Docetaxel was determined by analyzing the supernatant by UV-visible spectrophotometer at 229nm after suitable dilutions in ethanol. The percentage drug loading was calculated by using the following formula:

$$\text{Drug content (\%)} = \frac{\text{Conc. of drug loaded mesoporous silica}}{\text{Conc. of pure drug}} \times 100$$

Determination of drug loading:

Drug loading capacity of all drug loaded mesoporous silica were determined by suspending drug loaded mesoporous silica equivalent to 100mg of Docetaxel plain drug in 10ml ethanol (n=3).this suspension was then subjected to vortex (REMI ELECTROTECHNIK Ltd. DSC) for 15 min and then sonicated (CITIZEN LAB CD4820) for 10 min. The undissolved mesoporous silica was separated by centrifuging the suspension at 15000rpm for 10 min. Concentration of Docetaxel was determined by analyzing the supernatant by UV-visible spectrophotometer Concentration of Docetaxel was determined by analyzing the supernatant by UV-visible spectrophotometer at 229nm after suitable dilutions in ethanol. The percentage drug loading capacity was calculated by using the following formula.

$$\% \, drugloading = \frac{\text{Amt. of drug added - Amt. of drug in supernatant}}{\text{Amt. of nanoparticles}} \text{ X } 100$$

DRUG RELEASE STUDY:

The release of Docetaxel from Mesoporous silica nanoparticle was determined by the dialysis bag method. The DTX, DTX-PC, DTX-NPs, DTX-PCSD (equivalent to 60mg of DTX) were dispersed in 1 ml of water and placed into cellulose ester dialysis bags. The dialysis bags were immersed in 900ml release medium i.e. 1.2 pH phosphate buffer to determine drug release in stomach for 2 hrs and then in saline 7.4 phosphate buffer to determine drug release in intestine, containg 0.1%(v/v) Tween 80 carried out using USP paddle-type dissolution apparatus at a rotation speed of 100rpm, and at the temperature of 37±0.5°C.At predetermined time intervals, 10 ml of release sample was withdrawn, followed by supplying the same volume of fresh PBS solution. Drug concentrations of the samples were analysed by UV-Spectrophotometer at 230 nm.

IN-VITRO PERMEATION STUDY

Everted gut sac technique was performed to investigate the effect of DTX, DTX-PCSD and DTX-NPs on the absorption and efflux characteristic of small intestine *in vitro.* Male Wistar rat weighing 180-220g were treated in accordance with the guidelines of the animal ethics committee.

Rats were killed by cervical dislocation. And an approximately 10cm section from the small intestine was collected and flushed with K-R buffer.

In the mucosal to serosal (M-S) transport, the intestinal sac was tied at one end, filled with 2ml of drug solution (equivalent to 150µg of DTX), and then tied at the other end. The intestinal sac was

incubated in 10ml of K-R buffer solution maintained at 37°C. At each time interval, 5ml of the sample was withdrawn from the medium and replaced by an equal volume of fresh medium. Each sample concentration was determined by UV spectrophotometer.

Reverse serosal to mucosal (S-M) study was also conducted using the same method, except that the intestinal sac was everted onto a glass rod.

Papp= [$\frac{V}{A \times T}$] $\times \frac{C1}{Co}$

Where, V= Volume (ml) of serosal/mucosal content

A= Area (cm2) of small intestine

T= Time in sec

Co= Initial DTX Conc.

C1= Final DTX Conc. Estimated at determined time intervals

RESULT AND DISCUSSI

UV Spectrophotometric Analysis

The drugs sample of Docetaxel shows the λmax at about 229nm which complies with the reported literature.

- The UV spectra of drug in saline 7.4 Phosphate buffer.

Table no 4 **Standard Calibration Curve:**

Sr. No.	Concentration	Absorbance
1.	10	0.197
2.	20	0.322
3.	30	0.513
4.	40	0.684
5.	50	0.871

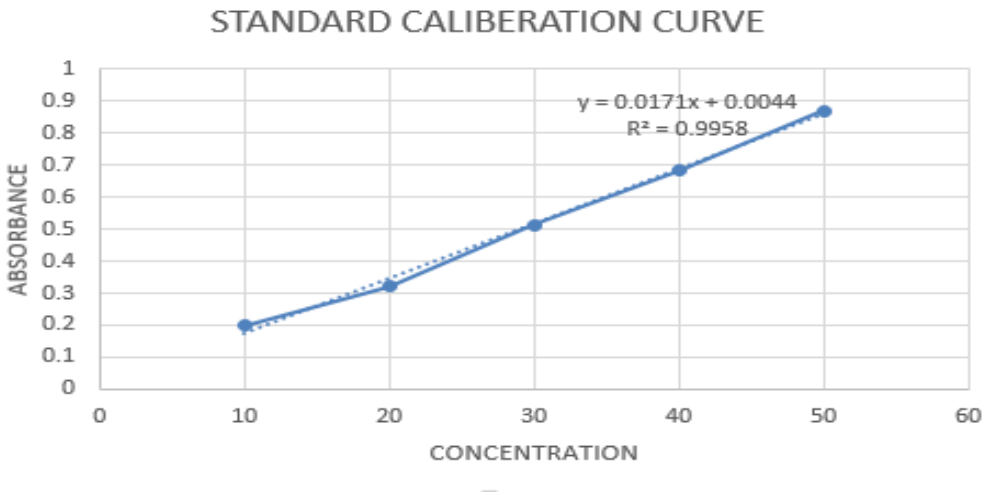

Fig. No. 4 Standard Calibration Curve

Table no 5 The UV spectra of drug in Ethanol:

Sr. No.	Concentration (ppm)	Absorbance
1	100	0.039
2	200	0.064
3	300	0.093
4	400	0.145
5	500	0.18

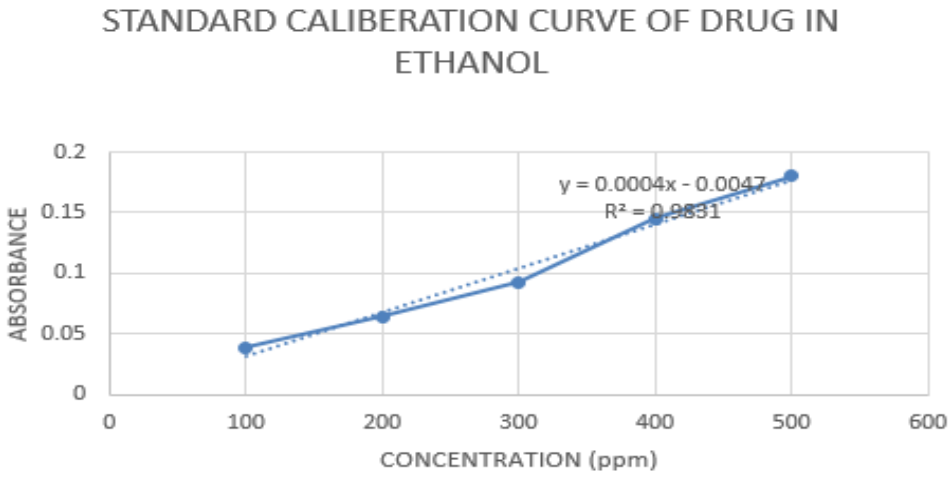

Fig. No. 5 Standard Calibration Curve of Drug in Ethanol

Table no 6 The UV spectra of drug in K-R buffer solution

Sr. No.	Concentration	Absorbance
1	10	0.028
2	20	0.064
3	30	0.092
4	40	0.154
5	50	0.177

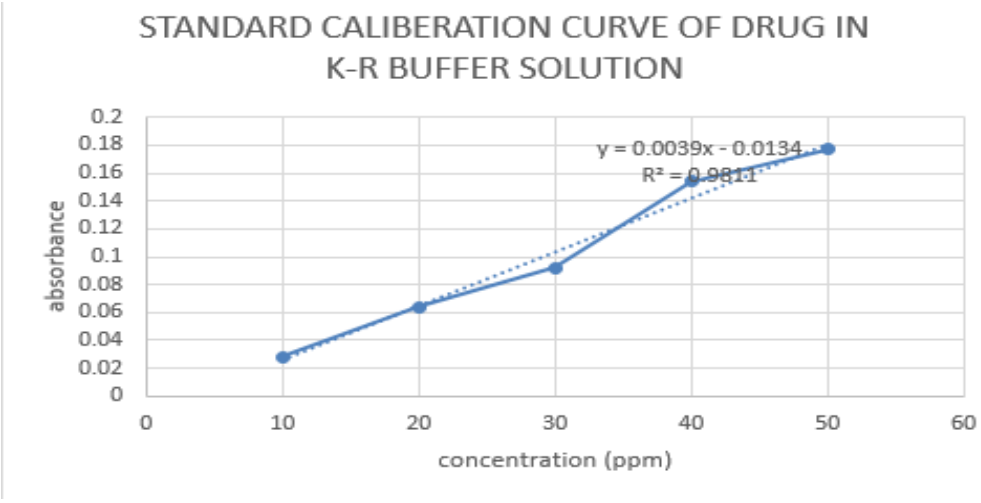

Fig. No. 5 Standard Calibration Curve of Drug in K-R Buffer Solution

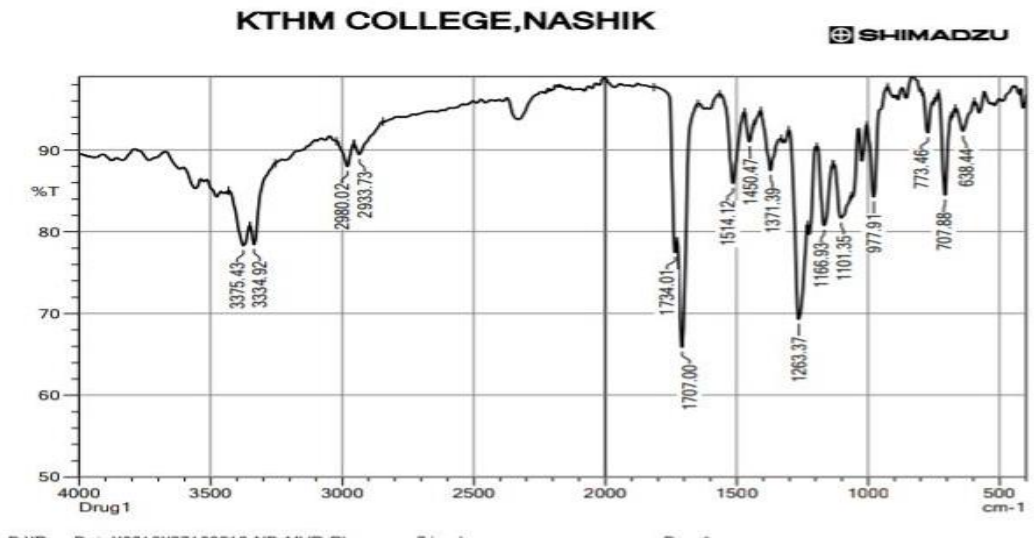

Figure no 6 ATR SPECTRA OF DRUG DOCETAXEL

Table 7 Interpretation of ATR spectra of drug DOCETAXEL

Frequency (cm-1)	Range (cm-1)	Group
3375	3200-3600	O-H
2980	2850-3000	C-H
1734	1734-1750	C=O
1101	1000-1300	C-O
1450	1450-1375	CH3
1263	1000-1350	C-N

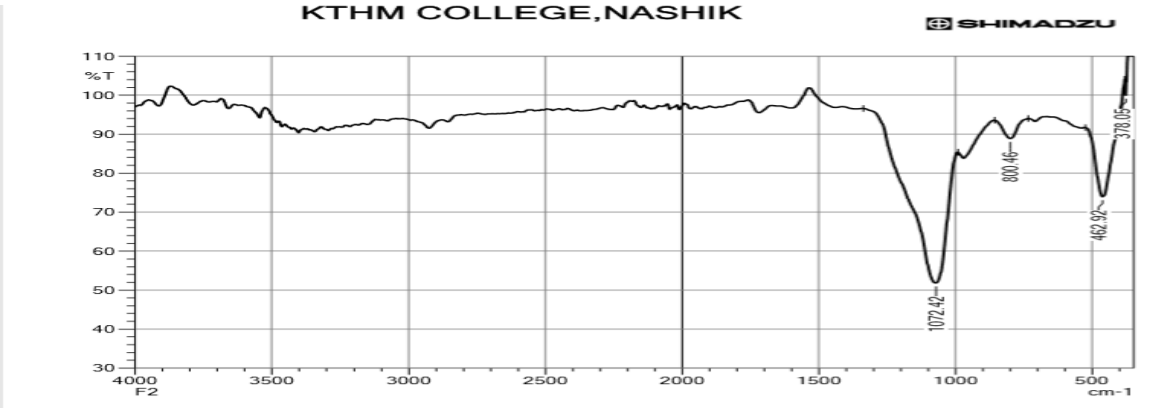

Figure 7 ATR SPECTRA OF MSN

Table no. 8 interpretation of ATR spectra of MSN

Frequency (cm-1)	Range (cm-1)	Group
1072	1050-1150	C-O
800.46	900-690	Aromatic

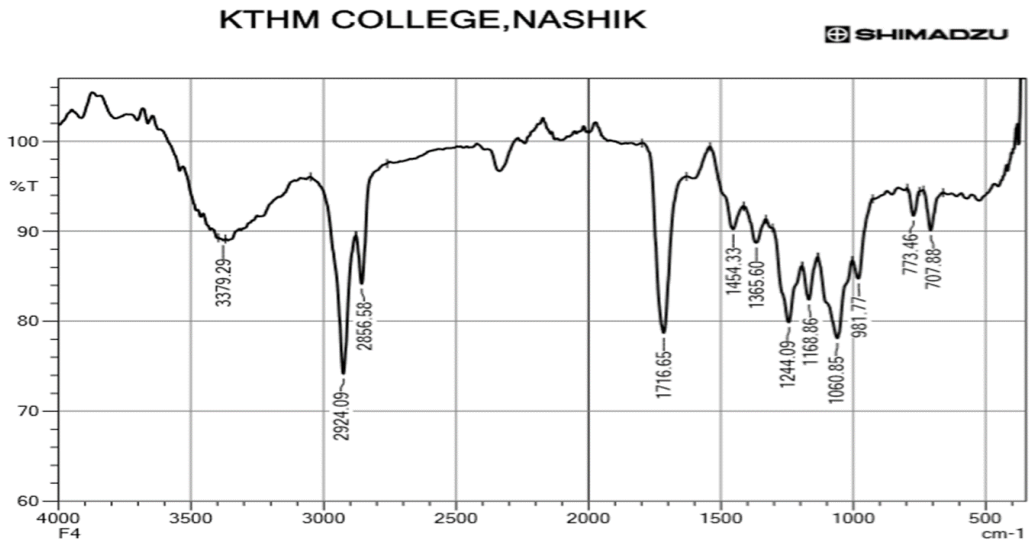

Figure no 8 ATR SPECTRA OF DRUG PHOSPHOLIPID COMPLEX

Table no. 9 interpretation of ATR spectra of Drug phospholipid complex

Frequency (cm-1)	Range (cm-1)	Group
3379	3200-3600	O-H
2924	2850-3000	C-H
1716	1705-1725	C=O (KETONE)
1454	1450	CH_2 (bending)
1355	1375	CH_3 (bending)
1244	1000-1350	C-N (AMINE)
1168	1000-1300	C-O (ESTER)
1060	650-1000	C=C (ALKENES)
773	690-900	AROMATIC

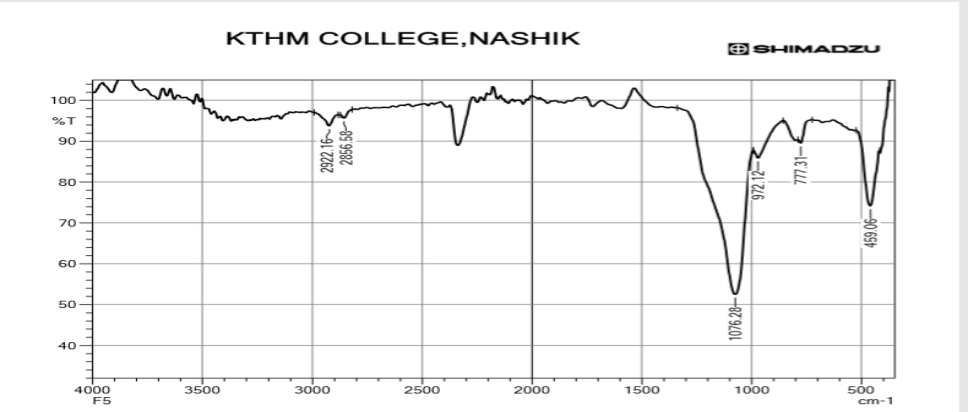

Figure no. 9 ATR SPECTRA OF DRUG PC-SD

Table no. 10 interpretation of ATR spectra of Drug-PC-SD

Frequency (cm-1)	Range (cm-1)	Group
2922	2850-3000	C-H (ALKANE)
972	650-1000	C=C (ALKENE)
1076.28	1050-1150	C-O (CARBOXYL)
777	690-900	AROMATIC

DSC Study

DSC thermograms of unformulated DTX, Physical mixture of DTX-PC and MSN, formulated DTX-PCSD are illustrated in fig.

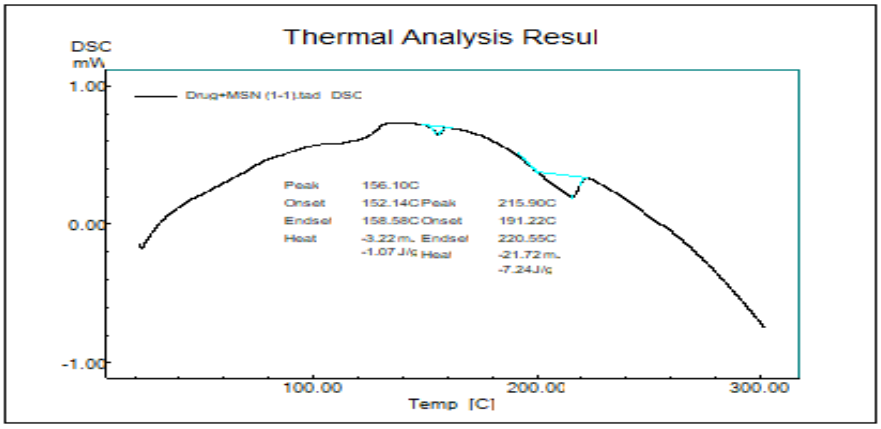

Figure no 10. DSC Thermogram of drug Docetaxel

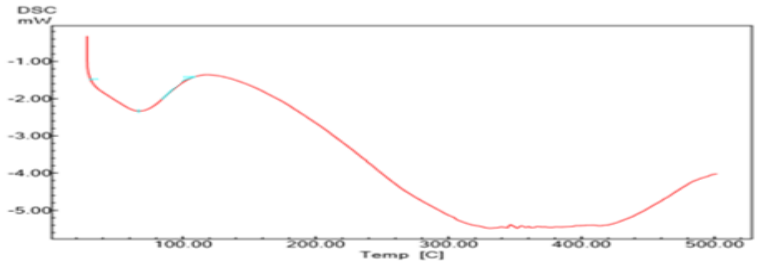

Figure no 11.DSC Thermogram of MSN

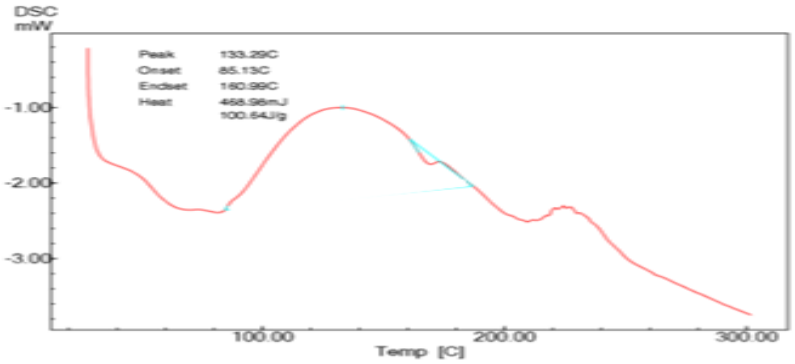

Figure 12. DSC graph of physical mixture Of DTX-PHOSPHOLIPID AND MSN

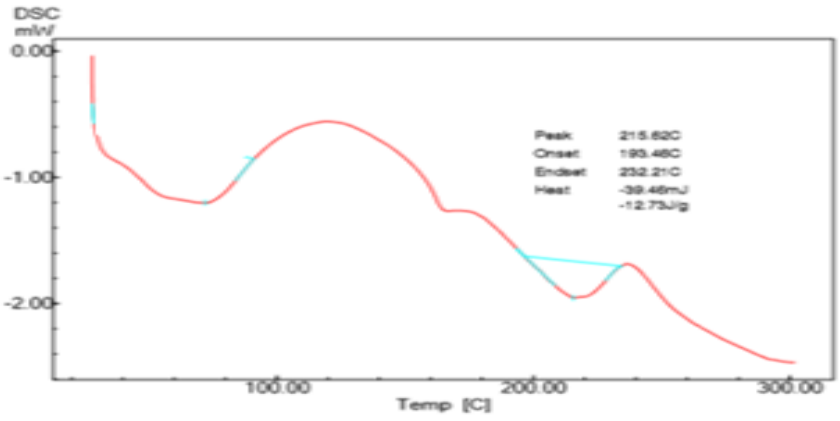

Figure 13. DSC graph of formulated DTX-PCSD

- As shown in figure, DTX exhibited a typical endotherm at approximately 190°C indicative of its anhydrous nature. The typical peak of DTX can be seen clearly in the DSC curve of the physical mixture of unformulated DTX-Phospholipid and MSN, but the melting point was decreased to 160°C and peak intensity was reduced. This phenomenon was caused by the partly complexing of the mixture during the melting process on DSC.

- Since the melting point of Mesoporous silica are too high to be shown in DSC study, flat curves without endothermic peaks confirmed the stability of the silica carrier.
- And in the DTX-PCSD formulation, the endothermic peak showed at approximately 190°C.

Scanning Electron Microscopy:

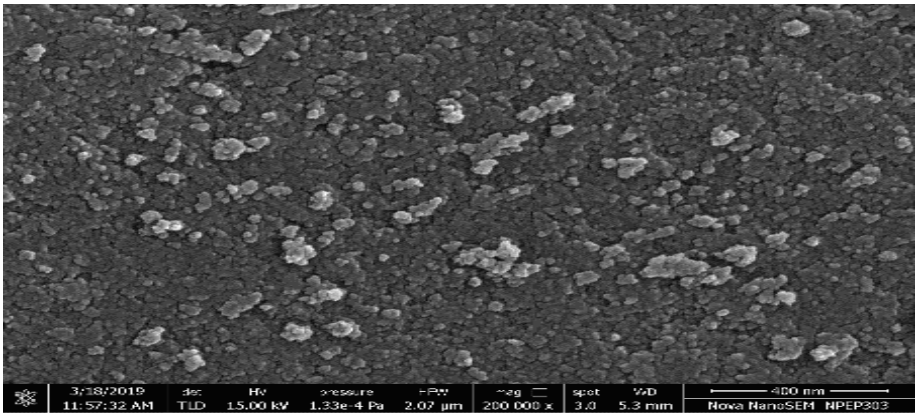

Figure no 14: SEM image of MSN

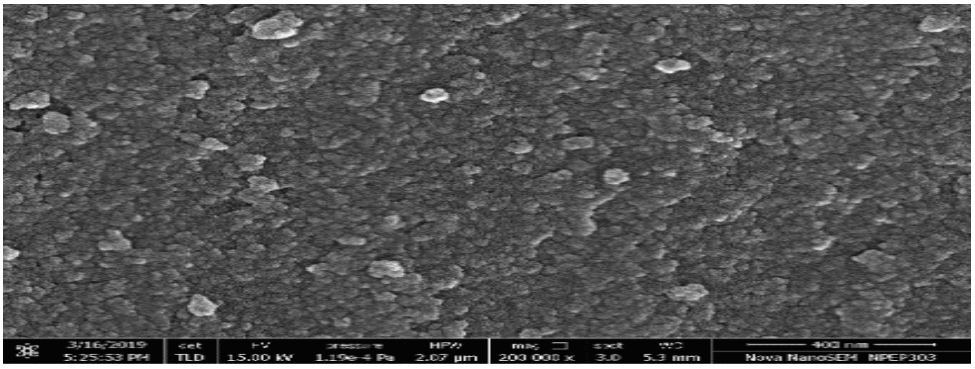

Figure no 15: SEM image of DTXPC-SD

The surface morphology, size and size distribution of the drug loaded nanoparticle were similar with those of the mesoporous silica as shown in the above figure.

Powder X-ray diffractometry (PXRD):

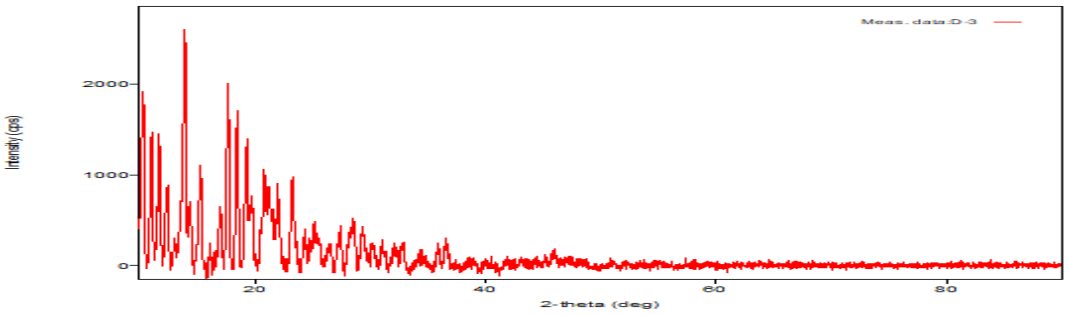

Fig no 16. PX-RD of drug Docetaxel

Table no. 11 interpretation of PX-RD data of Docetaxel

S. NO	2- theta (deg)	Rel. int. (a.u.)
1	10.315	66.34
2	11.719	38.29
3	13.935	100
4	15.296	34.21
5	17.679	58.66
6	19.696	27.52
7	24.293	8.66

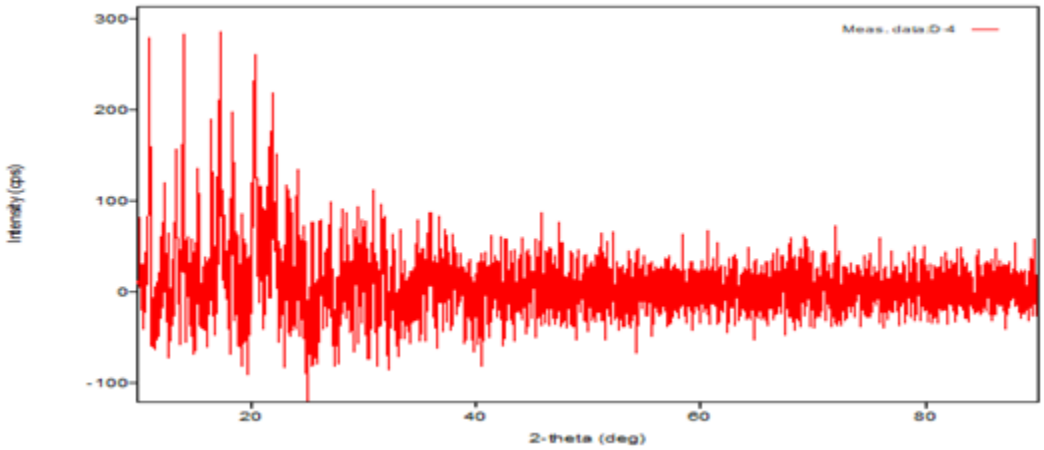

Figure no 16. PXRD graph of DTX PC-SD

Table no. 12 Interpretation of PX-RD data of DTX-PC-SD

Sr. NO.	2-theta (deg)	Rel. int. (a.u.)
1	10.971	40.38
2	15.316	16.16
3	17.29	86.97
4	21.97	100
5	32.617	5.11

Docetaxel showed various distinctive characteristic peaks. For DTX PC-SD, the diffraction peaks of docetaxel were disappeared, which indicated that Docetaxel was in non-crystalline or amorphous form after loading into mesopores because of the restriction of pore channels.

IN VITRO DISSOLIUTION STUDY

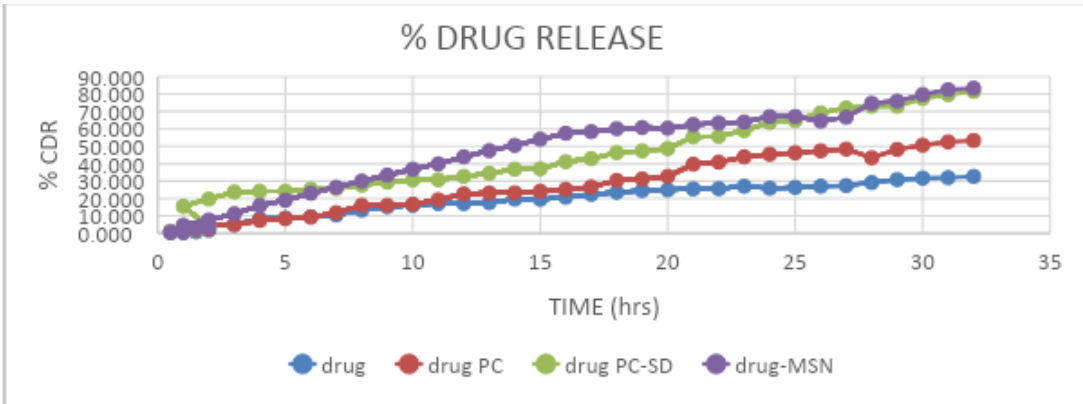

Fig. No. 17 % Drug Release

As results, DTX exhibited a dissolution percentage of 32.683±0.157% within 32hrs, while DTX-PC had significantly increased the percentage by 53.323±1.03%. The accumulative dissolution percentage of DTX from DTXPC-SD reached 81.601±0.364% within 32 hrs.

IN-VITRO PERMEATION STUDY

In- vitro Permeation study was determined by following formula:

Papp= $[\frac{V}{A \times T}] \times \frac{C1}{Co}$

Where, V= Volume (ml) of serosal/mucosal content

A= Area (cm2) of small intestine

T= Time in sec

Co= Initial DTX Conc.

C1= Final DTX Conc. Estimated at determined time intervals

Table 13 Everted gut sac technique is used to determine the penetration ability of drugs and carrier.

TIME(MIN)	60	120	180
drug(cm sec-1)	0.001688	0.002958	0.004087
Drug-MSN(cm sec-1)	0.001021	0.001139	0.001627
Drug PCSD(cm sec-1)	0.002285	0.008291	0.010077

Normal Sac technique:

Table 14 Everted gut sac technique is used to determine the penetration ability of drugs and carrier.

TIME(MIN)	60	120	180
drug(cm sec-1)	0.001590	0.001937	0.003158
Drug-MSN(cm sec-1)	0.000956	0.001492	0.003076
Drug PCSD(cm sec-1)	0.008787	0.008888	0.009969

CONCLUSION

- In summary, to enhance the oral bioavailability for BCS IV class drug Docetaxel , a system composed of phospholipid complex and ordered mesoporous silica- based solid dispersion was constructed using Docetaxel as model drug.
- The results showed that solubility, absorptive permeability on rat intestine by everted sac technique transport have been improved due to phospholipid complex, while in vitro dissolution rate dramatically increased by ordered mesoporous silica- based solid dispersion.
- Nanoparticles of Docetaxel using mesoporous silica loaded phospholipid complex for effective treatment in Cancer patients revealed following conclusion:

- The sample of drug and carrier received were found to be as per standards by preliminary characterization.
- In PXRD study, Docetaxel showed various distinctive characteristic peaks. For DTX PC-SD, the diffraction peaks of docetaxel were disappeared, which indicated that Docetaxel was in non-crystalline or amorphous form after loading into mesopores because of the restriction of pore channels.
- In SEM study, the surface morphology, size and size distribution of the drug loaded nanoparticle were similar with those of the mesoporous silica.
- DSC Thermogram of pure drug (Docetaxel) showed sharp endothermic peak at 190^{O}C, indicating melting point of Dapsone. On the other hand, there is no shifting in melting point endothermic peak in the DSC curve of drug PC-SD indicating that there is no change in the drug structure.
- Compared to that of unformulated DTX, in vitro drug Dissolution rate of DTX from DTXPC-SD significantly increased.
- Evaluations on rat intestine by Everted sac technique revealed that DTX-PCSD exhibited a significantly increased absorptive permeability compared to unformulated Docetaxel.

These results indicated that drug PC-SD can be a promising drug delivery system to enhance the oral bioavailability of BCS IV class drugs.

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