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NIOSOME BASED TRANSDERMAL FILM AS A NANOVECTOR FOR THE DELIVERY OF PACLITAXEL FOR SKIN CANCER

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ABSTRACT

Several topical creams to treat skin cancer have been used to deliver the drug of interest but it has been accompanied by various side effects. Novel drug delivery systems (NDDS), due to its small size and high specificity serve as a worthy opportunity for targeted drug delivery. This work aims at the synthesis and characterization of niosomes, which are phospho-lipid moieties having a 3D hollow structure. Different surfactants in various ratios were used initially to determine the best to load Paclitaxel (PTX), a chemotherapeutic drug proven to be a mitotic inhibitor. Niosomes of a uniform size of 100 nm have been synthesized on which FTIR, UV, Zeta Potential and Optical photomicrographic studies have been performed. An entrapment Efficiency (EE) of about 80.5% was achieved proving that the drug loaded niosomes have excellent pharmacokinetics. To facilitate topical application of PTX, a hydrogel was prepared using Carbopol 940 which gave a good release profile. Sustained release of drug requires constant contact to the target area, hence, in order to focus on sores which are perfused highly by tiny blood vessels, a transdermal film has been fabricated and its release has been measured.

KEYWORDS: **Paclitaxel, transdermal drug delivery, niosomes, entrapment efficiency, transdermal drug delivery**

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INTRODUCTION

Cancer is a bio complex phenomena which has several biochemical entities contribute to its growth and proliferation throughout the body[1]. Several methods are used to treat cancer and arrest its malignancy, like stem cell therapy, hormone therapy, targeted therapy, chemotherapy and radio therapy, to enlist a few. Of all these types of therapy, chemotherapy becomes the ultimate treatment course opted by the physician[2]. Cancer which manifests itself in various parts of the body like – breast, pancreatic, lung , ovarian etc. which claims several lives each year globally and is a serious threat to mankind[3]. Skin cancer exhibits itself as 2-3 million non-melanoma cases worldwide. This abnormal growth of cells in the basal or the squamous epithelia of the skin is prone to detach itself from the site of eruption to other parts of the body[4]. A transverse cross-section of the skin would reveal the 4 main parts of the skin, being – epidermis, dermis, subcutaneous/hypodermis and finally the nerve endings.It has been reported that over exposure to UV radiation acts as an environmental carcinogen which is responsible for producing Reactive Oxygen Species (ROS)[5]. Since DNA absorbs UV radiation at 245-290nm, it forms pyrimidine –dimers and photoproducts which in-turn delay transcription and activate various cell surface receptors. Pro-inflammatory cytokines flag off p38 MAPK cascade. Tyrosine kinases start up the Ras which follows the Raf downstream pathway producing MAPK-Kinase and finally MAPK. Irrespective of the type of UV radiation, research has shown that its exposure to human keratinocyte cells exhibit higher activity of p38 thus resulting in damage at the molecular level. Additionally, TNFα, a cell signaling protein, initiates immunosupression on exposure to UV-B. Therefore, TNFα involvement in the level of immuosupression is said to be directly linked to various causative factors such as the dose of UV radiation and the influence of other cytokines. It has been observed that people across the globe, be it dark or light skinned are affected with different forms of skin cancer. Skin carcinoma generally exhibits itself as a mole or a reddish patch sometimes having characteristic ulceration. It can be easily detected with a normal physical examination followed by a biopsy which reveals abnormal cell growth[6–8] .Treatment options for skin cancer range from cryosurgery to photodynamic therapy where a YAG laser is used to abalate the tumor site. Superficial squamous cell carcinoma is currently treated topically by 5-FU (5-Flourouracil), diclofinac and imiquimodare administered as semi-solid formulations[9]. Nanotechnology has played a crucial role in cancer therapy by contributing to the formulation of tiny particles in the form of nanovectors which carry the drug across the skin. Of carbon nanotubes[10], micelles[11], dendrimers[12], for drug delivery, lipid formulations top the charts as drug loaded nanovectors. They are said to have an advantage over the conventional therapy as these carriers do not loose their integrity during penetration and also are highly specific to the site of delivery on functionalization. Paclitaxel ($C_{47}H_{51}NO_{14}$), a crystalline, low molecular weight drug and is one of the best known antinioplastic drugs administered as a combinational therapy for the treatment of cancers. It is said to disrupt the overall functioning of the cell by initially starting with disturbing the dynamic equilibrium of microtubules, which is then followed by low cell motility and transport, formation of spindle fibers and finally cell death[13,14]. PTX has been proven to act on wide range of cancers such as breast, ovarian, lung, gastrointestinal, prostrate and also Kaposi's sarcoma.As it is highly lipophilic drug, it has a low aqueous solubility of 0.3µg/ml. Commercially available Paclitaxel IV is formulated with 1:1 ratio of a castor oil derivative known as Cremophor EL ,which has been proven to have a wide range of side effects such as hypersensitivity, peripheral neuropathy, nausea and healthy cell necrosis. Knowing the present drawbacks of PTX-IV formulation, vesicular systems have been the recent focus of research. These entities are basically formed by the rearrangement of diverse amphiphilic units on interaction with water[15,16]. These units assemble themselves into a single or multiple concentric lipid layers, finally forming a highly ordered and stable 3D structure capable of drug transport. The simplest of such vesicles are known as liposomes which are formed by the uniform arrangement of hydrated bilayers of a phosphilipid in water[17].Some of these vesicles namely liposome, niosome and ethosomes have been used as 3D carriers for essential drugs due to its high selectivity, small size and targetability. There are various routes of administration of drug into the system viz. oral, subcutaneous, sublingual, transdermal etc. where diverse research has been continuously going on to improve the pharmacokinetics of the drug.Oral route, although popular, suffers some substantial drawbacks like drug disintegration in the Gastro Intestinal tract and undergoes 'first pass metabolism"[18]**.** Transdermal Drug Delivery System(TDSS) is an appealing alternative to avoid the drawbacks of earlier used drug delivery system. GI irritation, variation in metabolism rate and dosage are easily controlled by the use of nano-vesicular structures which effectively ship the drug through the stratum corneum of the skin. Being aware of the draw backs of PTX, niosomes have been chosen for the purpose of drug delivery. Niosomes are non-ionic surfactant based vesicles formed by the self assembly of aqueous media- dispersed non ionic amphiphiles finally forming a 3D cage like structure. This unique structure facilitates the encapsulation of hydrophobic or hydrophilic drugs with respect to the surfactant being used. In drug delivery applications, the use of non- ionic surfactants has a hands-down advantage over anionic or cationic surfactants on the stability, bio-distribution[19,20].Niosomes have been used to effectively encapsulate various drugs such as itraconazole[21], doxorubicin[22], maxifloxacin[23] . Proteins such as human influenza vial antigens, Gn-RH based growth factors, vasopressin, insulin have also used niosomes as 3D carriers. This study takes into account the dispersion of paclitaxel loaded niosomes into a mesh like support known as carbopol to be directly applied to the site of tumor[24]. Gel based niosomes, due to its small size and high surface area is able to penetrate the tight junctures of the skin and move into the blood vessels which supply nutrients to the tumor [24-27].The primary focus of this paper is to assess the pharmacokinetics of PTX entrapped niosomes.PTX has been loaded onto the niosomes by way of handshaking method and dispersed into a topical gel for easy application. A transdermal film

has been prepared to act as a storage layer to the gel–containing niosome for constant delivery of chemotherapeutic drug to the tumor site. From the release rate studies of the drug loaded hydrogel, it was inferred to be suitable for prolonged use and that the niosomes would travel through the skin. Paclitaxel being a low molecular weight hydrophobic drug showed good entrapment efficiency of 80.5% with a higher concentration of surfactant to phospholipid source suitable for a transdermal drug delivery system.

MATERIALS AND METHODS

Materials Used

Span 60 and Soy Lecithin were purchased from Sigma Alderich, India. Tween80 and Cholesterol were purchased from LobaChemie, (India). Semi permeable membrane of cellulose acetate was purchased from Sigma AlderichLabware (India).Ethanol& chloroform were of analytical grade and used as such without further purification. Milli-Q water of resistivity 18MΩ was used for synthesis.

Niosomal Preparation

Niosomes were prepared by thin film hydration method. Surfactant and phospholipid are taken in a in a specific ratio and dissolved into an organic volatile organic solvent. In this paper, soy lecithin and cholesterol were used as the phospholipid (PL) sources, whereas Tween 80 and Span 60 were used as surfactants. Different formulations were transferredinto a 100 ml round bottom flask, slowly hand shaken at 80^0C until the film was formed. The film was later maintained in a vacuum desiccator to remove off excess moisture for a period of 2-3 hours. After cooling, the residual film was rehydrated with PBS (Phosphate Buffer Solution) to obtain the niosomes, maintained at room temperature in an orbital shaker until the film disappear and a cloudy solution was obtained. On evaluating the best formulation, PTX was loaded onto the niosomes by gently shaking 1mg/ml concentration of PTX solution for 30 mins in an orbital shaker kept at a constant RPM. Due to its lipophilic nature, PTX tends to accumulate between the double layers of the phospholipid tail groups. The excess drug was washed and removed. The niosomal solution was stored at 4^oC.

Preparation of PTX loaded niosomal hydrogel

To facilitate easy application and to enhance the drug's permeation ability through the skin, a hydrogel of the drug loaded niosomes was prepared. Definite amount of Carbopol 940polymer obtained by heating it in water at 60^0C,was sprinkled into the vortex created by stirring distilled water for a period of 25-30 min. 6ml of known concentration of niosomal suspension was added during polymerization to form the hydrogel. The gel was maintained at 6^0C over night for the vesicles to swell.

Preparation of Goat Ear Skin

Freshly slaughtered goat ears were obtained and initially cleaned under running tap water, which was succeeded by excising the dorsal skin from the underlying cartilage using a scalpel. The hair and subcutaneous fat was trimmed off using surgical scissors to expose the full thickness of the skin. The skin was immediately washed with DI water and placed into a Franz Diffusion cell for further studies. The excess skin samples were frozen at -4^0C, wrapped in filter paper wetted by saline and wrapped in aluminium foil. When skin samples were needed, they were taken out of the freezer, thawed and placed in the Franz Diffusion Cell for drug delivery studies.

Preparation of Blank Alginate Film

Sodium Alginate (SA) blank films were prepared by solution casting method. Being a biopolymer in powder form is first subjected to vigorous magnetic stirring after dissolving 3%w/v in DI for a period of 1 hour. Meanwhile, petri dishes of diameter 7.4cms were washed and kept dry to cast the SA gel. A thin layer of the gel is later poured into then petridish to form a uniform layer. As a gelating agent 3ml of $CaCl_2$ was used for 5 ml of SA gel. The calcium chloride behaves as a cross-linker and forms a film at room temperature. Once the film was formed, it was carefully peeled off from the petridish, and dried to yield a soft film. The film was later dried and stored at 10^0C wrapped in aluminum foil for further studies.

Characterization of Niosomes

Morphology

Optical Photomicrograph

The thin film formed at the bottom of the round bottom flask after hydration was re-dispersed in PBS and a tiny drop of it was placed on a clean glass slide. The glass slide was previously cleaned thoroughly with water and ethanol. The dispersion was observed under light microscope (Medilux-207R (II), Kyowa-Getner, India), with a magnification of 1200x and captured by Olympus E-5 DSLR camera.

Sem

Surface morphology of the niosomes like, shape and size were determined using SEM (Scanning Electron Microscope). In the case of SEM analysis, a drop of sample was added to an aluminium foil and dried overnight in a desiccator to remove all the excess moisture. It was then subjected to electron beam (Quanta FEG Bruker) which determined the size and morphology of the as synthesized niosomes. The sample was analyzed in low vacuum at various levels of magnification.

Size and Zeta Potential Measurements

DLS studies were performed on diluted empty niosomes, using Malvern Instruments Ltd. Zeta Potential v2.3 to determine the size distribution and average vesicle profile of the synthesized vesicles.Dilution was required to remove unwanted agglomeration which might have occurred between two adjacent niosomes.

Niosome Aging Process

Aging process of niosomes is determined by storing the as-synthesized vesicles at near freezing temperature (4^oC) with the help of an incubator freezer over a period of 4 weeks. Every 6^{th} day, the niosomes were thawed and brought to room temperature. UV Spectrophotometry was performed at 230nm to determine the drug retention capacity and leakage of vesicles. The amount of drug released could be

analyzed by change in absorbance. No physical changes, viz, clouding, agglomeration or flocculation was observed by the naked eye.

Fourier Transform Infrared Microscopy (FT-IR)

For FTIR studies, the as prepared niosomes were removed from its suspension by centrifugation at 8000 RPM and dried under reduced pressure using a rotary evaporator. The dried sample containing the best ratio of niosomes was dried and added to KBr powder and subject to hydraulic press to make thin pellets. The Infrared spectra was obtained using Bruker Alpha FTIR on empty niosomes, bare PTX and PTX loaded niosomes for comparison.

pH of the Gel

Determining the pH of the formulated topical gel is an important parameter to measure as it comes in direct contact with the skin. High pH would irritate the pores of the skin and would render uncomfortable for application. pH of the gel was studied using a pH paper.

Determination of Niosomal Encapsulation Efficiency

The drug encapsulated study is one of the most vital aspects of drug loading and delivery. In this study, the vesicle samples were procured and subjected to centrifugation at 13,000 RPM using **Remi R4C**. The niosomes were washed once again with DI to remove excess drug.The supernatant which would give the amount of the un-entrapped drug was considered as drug loss and subjected to UV Spectroscopy studies. The pellet acquiredon centrifugation was washed with 5ml of 50% iso-propanol and placed in a mechanical vortex to dissolve it completely. The dissolved pellet was re-centrifuged at 4000 rpm to separate the drug from lysed vesicles and subjected to UV studies at λ_{max} 230nm to evaluate the drug loaded into the niosome.

Where,

R – Amount of drug released from Vesicle

O – Original amount of drug taken

$$\text{Entrapment efficiency} = [(O-R)/O]*100$$

In –Vitro Drug Release Kinetics

Dialysis method was used to evaluate the drug release kinetics of the loaded niosomes. The membrane was first activated by 2 types of buffer solution consisting of EDTA and kept at 45^0C for a period of 20 mins. The membrane was later removed from the buffer solution and washed thoroughly with DI to remove the excess ions. Once activation was performed, drug loaded niosomal solution was filled in and the bag was immersed in 50 ml PBS. Niosomal suspension containing a known concentration of PTXwas filled into dialysis bags having a uniform porosity of 10mm. It was maintained at 7.4pH and stirred constantly at 100 rpm at 37^0C in buffer to check if the vesicles maintain their integrity at body temperature and to maintain sink condition. 3 ml solutions were drawn at regular intervals and replaced with fresh PBS and stored in separate vials for UV analysis. Each aliquot drawn were analyzed spectroscopically at 230nm to obtain a specific OD value.

Ex-vivo drug release kinetics on goat ear skin

Drug release studies also was conducted using Franz Diffusion cell. An evaluation of the drug release through a membrane which mimics the semi permeability of the layers of the skin is necessary for this study. A two chambered Franz diffusion cell was used having a 50ml receiver compartment capacity filled with PBS. The Franz Diffusion system was maintained at an rpm of 200 and a temperature of 37.5 ± 1^0C to mimic body temperature. To evaluate permeation studies, goat ear skin was placed between the donor and receiver compartments. Carefully, 3gms of prepared nano vesicle drug-loaded gel was spread over the goat ear skin, in the donor compartment and magnetic stirring was performed over various time periods. 3ml PBS was drawn at regular intervals and via capillary tube using a pistol syringe and equal amount of fresh PBS was replaced stored as aliquots, subjecting to UV spectroscopy for analysis.

Physical appearance of the transdermal film

The transdermal films were inspected for their flexibility, color, and smoothness over a period of time.

Thickness of the drug loaded polymeric film

Thickness of the polymeric film was determined using a screw gauge. For the 5 different films prepared, each one was measured and an average value was taken.

Surface pH of the alginate patch

As the patch would be in direct contact with the skin surface, it is important to evaluate the pH of the as prepared film. The surface pH was measured using pH paper.

Ex-vivo drug release kinetics on transdermal film

As for the release studies of hydrogel on goat ear skin, here too Franz Diffusion Cell was used to evaluate the amount of drug eluting out of the system. A known concentration of the drug in the form of hydrogel was applied onto the transdermal patch.

RESULTS AND DISCUSSION

In this study, niosomes of the combination of Cholesterol and Tween 80 in 1:2 ratio was chosen to entrap PTX due to its high entrapment efficiency and shape retention properties. Table 1 shows various trials performed on different phospholipids and surfactants and its entrapment efficiency along-with.

Table 1
Trials Conducted on different formulations

SAMPLE	PHOSPHOLIPID SOURCE	SURFACTANT	SOLVENT(ethanol: chloroform) (1:1)	Entrapment Efficiency (%EE)
N1	Cholesterol	Tween 80 (1:1)	5ml : 5ml	72.4%
N2	Cholesterol	Tween 80 (1:2)	5ml : 5ml	80.5%
N3	Soy Lecithin	Span 60 (1:1)	5ml : 5ml	66.8%
N4	Cholesterol	Span 60 (1:2)	5ml : 5ml	68.2%
N5	Soy Lecithin	Tween 80 (2:1)	5ml : 5ml	67.8%

Generally, polysorbitol 80s are said to have an HLB (Hydrophile – Lipophile Balance) index >10, which means it has lipid insoluble surfactant properties[26].Cholesterol, being a type of lipid molecule, a principal sterol synthesized by animal cells is used to maintain structural integrity and fluidity[27]. This lipid source is widely available and is known for its compatibility with the human skin. On the other hand, Tween 80 is a non-ionic surfactant and emulsifier used which occupies the interstitial spaces within the phospholipid moieties in a 3D vesicle[28]. A high percentage of entrapment would mean that less effort or energy is required to pass on the drug to the delivery to the target site. Tween 80 being a surfactant interacts with the stratum corneum of the skin, loosening up the tight junctions to allow easy movement of nanoparticle through it. Several methods have been employed over time and thin film hydration technique wasdetermined to be the best method for synthesis.Once the thin film was obtained at the bottom of the RB flask, the niosomes were rehydrated with cold PBS. The as synthesized niosomes were diluted 10 times to obtain clear morphological images. Optical photomicrograph (Fig 1a) and Scanning Electron Micrographs (Fig 1b) of the as prepared niosomes were taken as the initial test to determine the formation of niosomes in suspension.

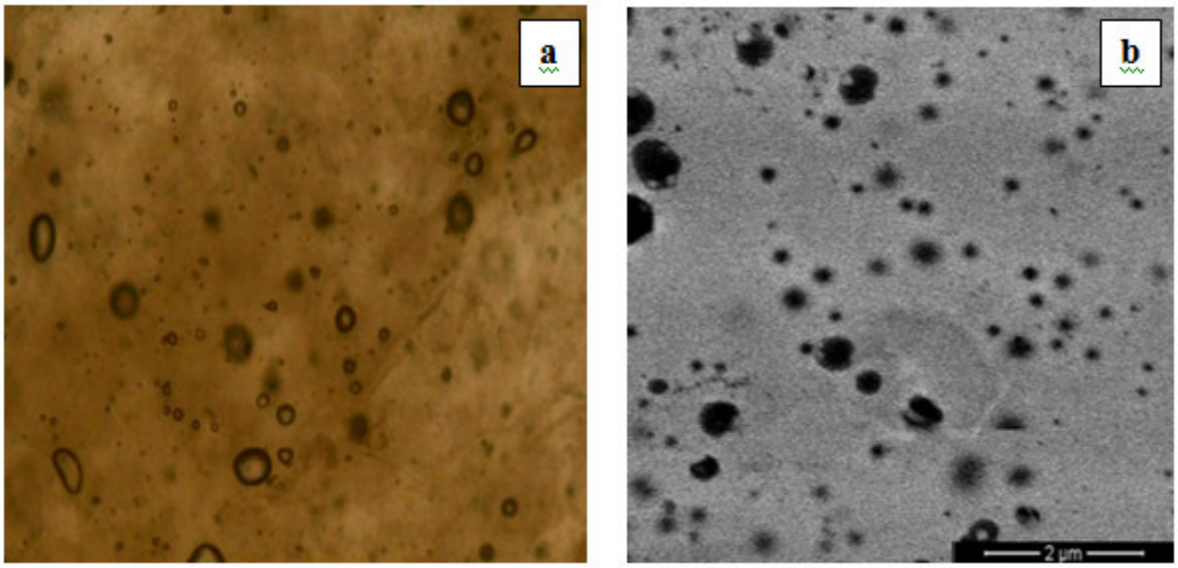

Figure 1
(a) Optical Photomicrograph of Niosomes (x1200) (b) SEM of as prepared Niosomes

SEM imaging and optical microscopy confirmed the spherical shape of the niosomes having a core diameter of around 200-250nm. The functional groups present in the niosomal system were evaluated using FTIR studies[29]. Since PTX is a highly lipophilic drug, logically it is supposed to occupy the interstitial spaces between the tail groups. FTIR studies performed exhibited the existence of functional groups at different wavenumbers over a range of 400-4000cm^{-1}.The FTIR spectrum given in Fig 2(a) showpeaks at 1707cm^{-1} and 711cm^{-1} characteristic of C=O group and PTX aromatic ring in accordance with pure PTX. Fig 2(b) illustrates the FTIR spectrum of empty niosomes where O-H bond stretching was observed at 3450cm^{-1} and a mild peak at 1600cm^{-1} depict the presence of ester bonds. CO stretching and C=O vibrations (1707cm^{-1} and 1450cm^{-1}) in Fig 2(c) representedthe integrity of the niosomes remained intact even after interaction with PTX. It is now evident that the phospholipid and surfactant molecules in conjuction with the PTX aromatic ring are bound through H bonding[30].

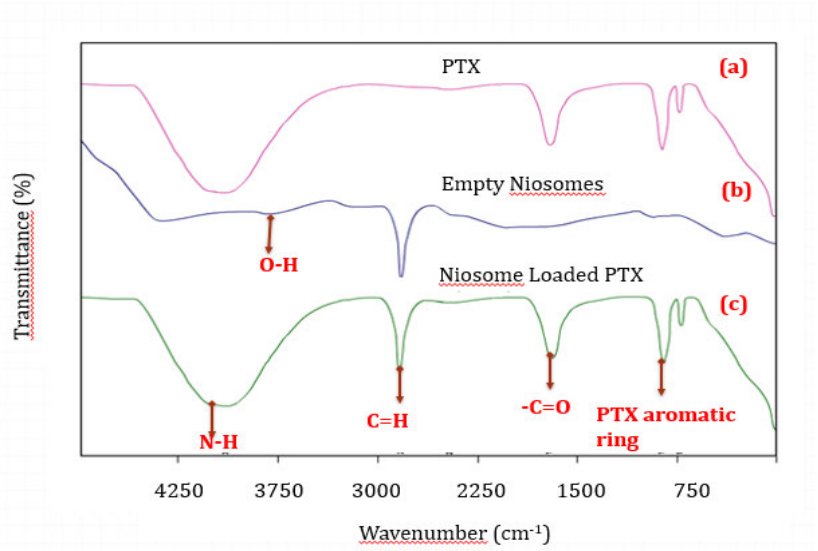

Figure 2
FT-IR spectra of paclitaxel (a), Empty Niosomes (b) and Niosome loaded with paclitaxel (c)

To investigate the influence of choice of surfactant and phospholipid source on the efficiency of drug loading into the niosomes, particle size was evaluated using DLS (Dynamic Light Scattering) technique on empty niosomes. The DLS values (Fig 3(a)) gave the size distribution of the niosomes to be around 200- 250 nm which are appropriate to penetrate the pores of the stratum corneum. The Zeta potential values, which is basically dependent on the surface charge of the lipid matrix, suggest a stable suspension of niosomes having potential of -28.6mV. Since particle size of the vesicles synthesized have a direct influence on the permeability and bio-distribution of the drug through the stratum corneum. Low molecular weight drugs encapsulated in small niosomes have a far more likely chance to penetrate the skin rather than bigger ones, substantially reducing the dosage. The Z-diameter shown in (Fig 3(b)) suggesting that the vesicles are of a uniform size range of 200nm on an average and the standard deviation was about 77 nm.

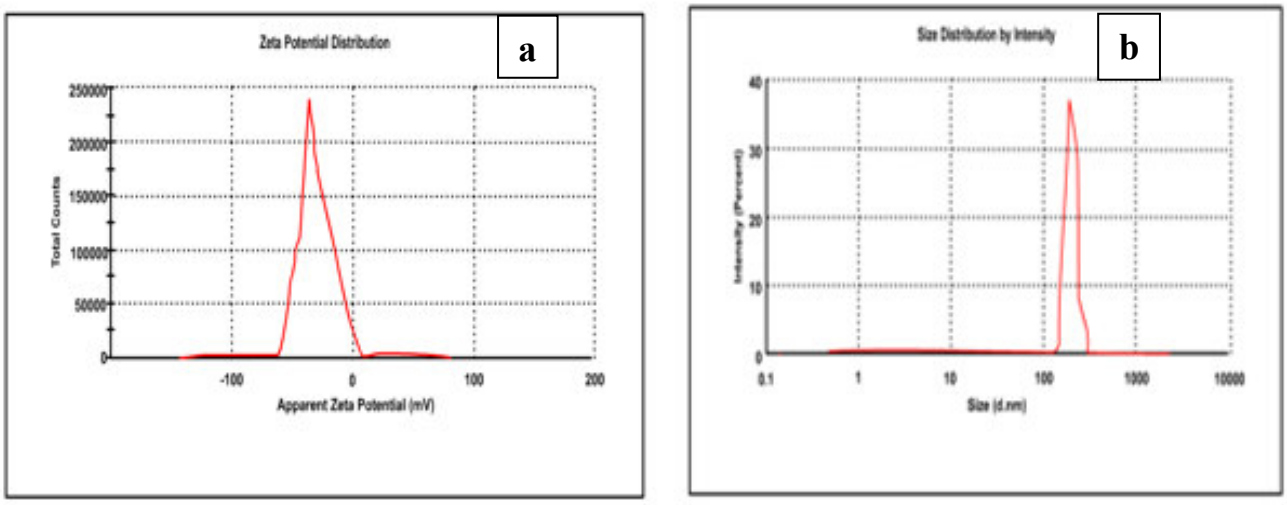

Figure 3
Zeta Potential for (a) As prepared Niosomes and (b) Size distribution study

Fig 4shows the UV pattern obtained for niosomes at 230nm,at regular intervals. No agglomeration or flocculation was found in the prepared suspension. This implies that the niosomes containing the drug maintained their closed 3D structure and its integrity did not diminish over time. Physical stability also revealed that the synthesized niosomes did not show any kind of drug leakage or instability in its structure when analyzed with the naked eye.

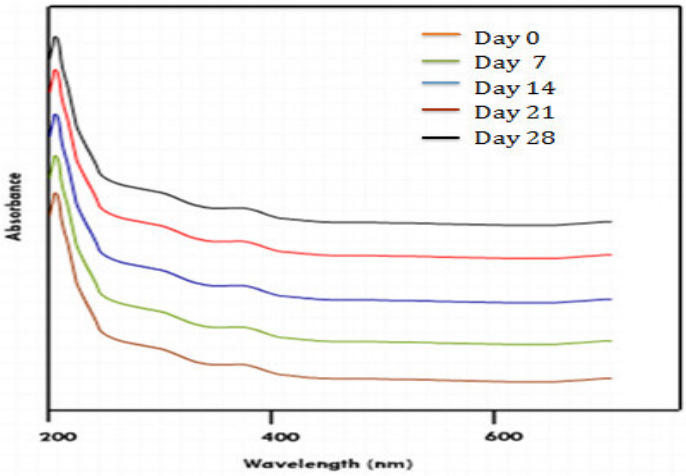

Figure 4
Stability studies using UV spectroscopy

Once the size and morphology were determined, release studies were performed where in PTX loaded niosomes were subject to centrifugation at 13,000 rpm and subject to UV analysis. The O.D obtained at 230nm showed that the amount of drug released and was estimated to be 80.5%.Drug release statistics provide insight to the interaction of drug loaded niosomes with PBS which hopes to strike an equilibrium with the receiving medium until all the drug has been eluted. The preliminary studies for release rate were performed using a standard dialysis bag immersed in PBS. The release rate showed a constant increase in graph until it peaked in the 1st5 hours and slowly reached saturation by 24 hours. This can be due to the fact that the set RPM, can influence the rate at which the drug is eluted out into the buffer solution. Preparation of a Carbopol 940 gel was done to support the niosomal suspension as it acts as a gauze over which niosomes would be lodged. The pH of the gel was checked so as to ensure it does not cause irritation to the skin surface. Study on its pH showed that the patch is slightly acidic, having a value of 6±0.5, which was compatible with the human skin. Choosing the goat ear skin for the ex-vivo studies is attributed mainly to its cartilaginous nature and presence of large number of blood capillaries[31].Fig 5 (a) shows the Franz diffusion cell set up which is designed uniquely, to perform the pharmaceutical release studies. The single outlet is used to constantly remove required amount (3ml) of the sample through it. Fig 5(b) shows the as prepared Carbopol hydrogel containing the drug loaded niosomes. Fig 5(c) shows thegel applied on the surface of the skin after preparation. Due to high skin receptiveness, permeation through the skin is an easier task. A similar but longer release profile was observed with the goat ear skin as that of the dialysis membrane. Carbopol acting as a matrix tends to release the drug with lower retention and the gel completed eluting all of the drug around 30 hrs, as given in Fig 5(d).No particular release profile was understood from that of goat ear skin as the release medium as it sought to reach equilibrium.Initial burst release was not found in gel bearing or dialysis mode of delivery because Tweens in a higher ratio to phospholipid source tends to withhold the vesicular structure and reducing leakage. A transdermal film was synthesized keeping in mind its easy usage as a patch for skin cancer and to ensure its effective bioavailability through the affected skin surface.

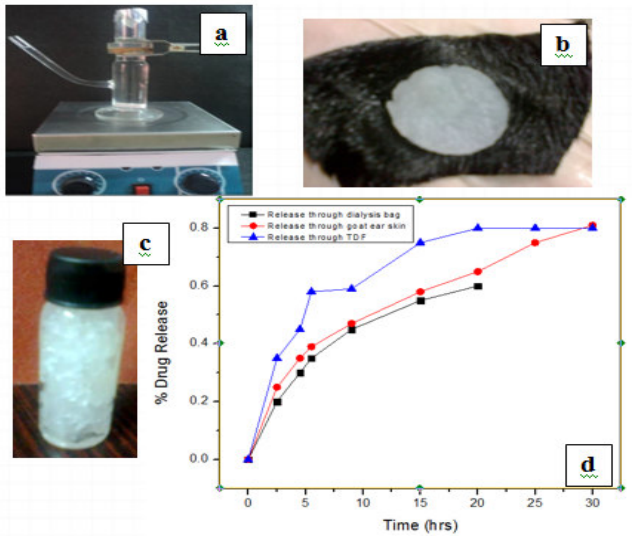

Figure 5
Franz Diffusion Cell (a) Goat ear skin with PTX hydrogel (b) PTX gel (c) Release Rate studies (d)

Sodium alginate is a natural polymer which has an ability to form a gel on heat application. Being an anionic polymer it is said to enhance drug delivery avoiding the first pass metabolism and also maintaining constant drug plasma levels[32]. In order to enhance the permeation of drug through the *stratum corneum*, a transparent sheet of sodium alginate was fabricated and the niosomal drug loaded hydrogel was spread onto it (Fig.6).

Figure 6
Sodium Alginate patch smeared with drug loaded hydrogel

The transdermal film (TDF) had a thin and transparent physical appearance and did not exhibit any kind of color change or shrinkage over time. TDFs were prepared and stored in batches for over 30 days at 4^0C and no hardening or breakage was noticed. Table 2 contains the weights and corresponding thicknesses of the prepared TDSs.

Table 2
Thickness and Weights of Sodium Alginate films

Sample No	Thickness of the SA Film (mm)	Weight (gm)
1	0.253±0.025	0.45
2	0.273±0.024	0.38
3	0.250±0.024	0.40
4	0.230±0.024	0.41
5	0.205±0.024	0.42

Surface pH is a very important factor to the patch as it remains in direct contact with the affected skin surface for a long period of time. The pH was measured to be 6.87±0.05 which is very much compatible to the skin. Release studies show a slightly varied pattern as compared to that of the hydrogel. The release of the drug peaks at 10hrs and reduces drastically. This might indicate rapid release profile more suitable for instant relief in a short period of time and a sustained amount of drug released with passing time. Evidently, then niosomes are able to permeate into the system through the SA patch and deliver the drug across the membrane.It is also possible that the rate of delivery can be controlled by changing in the thickness of the film or the number of layers contributing to making the final patch.These results suggest that a SA patch can be a good alternative to IV based chemotherapy for treating skin cancer.

CONCLUSION

In conclusion, PTX can be encapsulated into niosomes prepared from non-ionic surfactants to carry them across the skin barrier. The niosomes with an appropriate size of 200-250 nm could provide good penetration through the stratum corneum. The formulation containing cholesterol as the phospholipid source and Tween 80 as surfactant in the ratio 1:2 provided the best %EE of the various combinations. The niosomal formulation exhibited a good physical and chemical stability, entrapment efficiency and release rates.The results show that the initial release of paclitaxel increases with over a period of time and stabilizes as it reaches its saturation. The low solubility and lipophilicity of PTX has forced researchers to developa more suitable route to enhance the uptake, removing the harsh side effects of Cremophor EL® which is a caster oil based entity, generally complexed with PTX. To conclude, a patch of sodium alginate was used to act as a platform to load the niosomal formulation. These studies shows a prospective way to improve the bioavailability and hence the efficacy of PTX towards skin cancer treatment.

CONFLICT OF INTEREST

Conflict of interest declared none.

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