REVIEW OF HERBAL NIOSOMES

[1]V.Swetha, [2]Dr. G. Uma Rani

Department of pharmaceutics,
RBVRR women's College of Pharmacy,
Affiliated Osmania University, Hyderabad- 500027

***Abstract*: The objective of this study is to review the herbal niosomes.Niosomes considered as novel drug delivery systems, can improve the solubility and stability of natural pharmaceutical molecules. Niosomes are non-ionic surfactant vesicles which are obtained by hydration of synthetic non-ionic surfactants, cholesterol or other lipids. They are vesicular Drug delivery systems similar to liposome's that can be used as carriers of amphiphilic and lipophilic drugs. Niosomes are less toxic and improves the therapeutic index of drug by restricting its action to target cells. It provides recent data about the various types of herbal niosomal preparations, uses and their results with the improving availability of innovative natural methods to overcome diseases with herbal niosomes. Using new drug delivery system like niosomes are helpful in herbal formulations with reducing toxic effect and increasing therapeutic effects. These study gives data about some of the herbal niosomal formulations.**

***Keywords*: Niosomes, non-ionic surfactant, herbal niosomes, amphiphillic and lipophilic.**

NIOSOMES:

In niosomes the medication is encapsulated in a vesicle, composed of a bilayer of non ionic surfactants and cholesterol. Niosomes are novel drug delivery system and used as carriers of amphiphilic and lipophilic drug

IMPORTANCE:

Development of new drug, improving safety, efficacy of existing drugs is difficult, expensive and time consuming.

At present no available of drug delivery system behaves ideally achieving all the goals.

Encapsulation of the drug in niosomes, results in delivery of drug directly to the site of action, leading to the reduction of drug toxicity with no adverse effects.

WHY….

As niosomes are considered as appropriate carriers for anti-infective, anti-microbial, anti-inflammatory and anti-cancer drugs.

They are used as Targeted Drug Delivery system, improves oral bioavailability of poorly absorbed drugs, minimize drug toxicity and improve drug therapeutic and improve drug therapeutic indices.

BENEFITS:

Niosomes improves bioavailability of medication, solves the problems of drug insolubility, instability and rapid degradation and reduces cost of treatment

ADVANTAGES:

Targeted drug delivery can be achieved.

Reduced dose is required to achieve desired effect and decreases in side effects.

Niosomes are amphiphilic in nature.

Improve the oral bioavailability of poorly soluble drugs.

Enhance skin permeability of drug through topical administration, advantageous of usage through various routes oral, parenteral, topical, ocular.

Osmotically active & stable.

Surfactants used in niosomes are biodegradable, biocompatible, and non-immunogenic.

The therapeutic efficacy of the drug is improved by reducing clearance rate targeting to the specific site.

DIS-ADVANTAGES:

Inefficient drug loading.

Requires specialized equipment.

Time consuming.

Niosomal suspension may exhibit fusion, aggregation leaching, hydrolysis of entrapped drug, limiting the shelf life of niosome.

APPLICATIONS:

Niosomes have been used for oral delivery, transdermal delivery, ocular delivery, pulmonary delivery, nasal route, cancer therapy, gene delivery, drug targeting.

Immunological applications

Delivery of peptide drugs

Leishmaniasis treatment

Carriers for hemoglobin

Cosmetics.

REVIEW OF HERBAL NIOSOMAL FORMULATIONS

PHYTONIOSOME-A NOVEL DRUG DELIVERY FOR MYRTLE EXTRACT

In traditional medicine, the herbs has been used topically for the treatment of nosebleed, burn, mouth ulcer, wound & has been applied as an antiseptic and disinfectant remedy(1-2). There are some limitations for topical usage of the myrtle extract resulted from its poor biopharmaceutical properties, low solubility, and low permeability (3). So they developed a niosomal formulation which is beneficial for myrtle extract release and bioavailability in topical formulations. And to enhance the myrtle extract stability and permeability. Then the optimized formulation is evaluated for entrapment efficiency, size, release profile, stability studies to compare with the myrtle extract anti-bacterial & cytotoxicity activity. Niosomes are prepared by using film hydration technique (5). Firstly, the extraction process is done by isolating the myrtle leaves from the aerial parts of the plant and allow them to dry for one month. These dried leaves were grinded into a powder. Extraction is prepared by putting 100g of myrtle leaves into a percolator column to it ethanol 80% was added continuously and concentrated in a rotary evaporator at 45ºCand dried in a oven 40ºC. Then they determine the total phenol content in myrtle extract spectrophotometrically using Folin-Ciocalteu reagent assay with Gallic acid as standard with slight modifications (4). They determine the assay linearity as 150-500µg/ml Gallic acid equivalents. The concentration of total phenolic compounds in myrtle extract was determined as mg of Gallic acid/g of total extract by using regression equation obtained from the calibration curve of Gallic acid standard. Niosomes are prepared by film hydration method by using non-ionic surfactants including span, tween, and cholesterol in different ratios & dissolved in chloroform, ethanol with 2:1 ratio in a 1000 ml round bottomed flask. Then Myrtle Extract solution was added to the lipid phase. The organic solvents were removed under vacuum in rotary evaporator for 30 min to form a thin film on the walls of the flask. Residual solvents were evaporated & the film hydrated for 1 hr to produce niosomal suspension containing Myrtle Extract 4%.They formulated six niosomal formulations and performed evaluation tests. These preparations were evaluated for particle size, Zeta potential, Encapsulation Efficiency, Vesicle stability, phytoconstituents release and for antibacterial activity. They evaluated the particle size of phytoniosomes by using laser light scattering method in a Malvern particle size analyzer. And by using optical microscopy they found out the morphological differences between formulated phytoniosomes with different surfactant and molar ratios. They used Scanning electron microscopy for surface morphology, WALLIS zeta potential analyzer for zeta potential values. The phytoconstituents release evaluation is done by the Invitro release study which was performed by using Franz diffusion cell. Disc diffusion method is used to screen antibacterial activity in myrtle extract. The multilamellar vesicles were obtained from Span60/Tween60, Span40/Tween40. Surfactants in presence of cholesterol Span60/Tween60 with Myrtle Extract 4%was found to be the optimal formulations and was stable for more than 3months. Particle Size is 5.28±0.31µm, zeta potential is 25.33±1.40mV. Entrapment Efficiency% approximately 91.5%...reduces release rate & prolongs the duration of action, shows the lower toxicity effect and better antibacterial activity compared with Myrtle Extract.

FORMULATION OF NIOSOMAL GEL CONTAINING GREEN TEA EXTRACT

(CAMELLA SINENSIS L. KUNTZE)USING THIN LAYER HYDRATION:

They prepared a niosomal gel to overcome the problems of low permeation of active substance through the skin layers and to increase the stability. Green tea is known as source of antioxidants. Antioxidants(herbal) are skincare alternatives because of the skin nature & less adverse effects, allergic reactions when compared to synthetic ones. Niosomes are prepared by dissolving cholesterol in 50 ml of dichloromethane They prepared a topical antioxidant formulation to overcome the problems of low permeation of active substances through the skin layers & to increase their stability (16). To enhance the drug stability, Niosomal formulations were prepared in four different ratios of surfactant to cholesterol F1 (3:1) F2(2:1) F3(1:1) F4(0.5:1) using thin layer hydration technique. Niosomes are prepared by taking span 60 and cholesterol and dissolve it in a 50 ml of dichloromethane, placed in a round bottomed flask & evaporated in a rotary evaporator at 39ºC until the residuals are evaporated and thin film is formed. Then the film should be hydrated with phosphate buffer solution to form niosome preparation. The gel was prepared by dispersing the polymer in aqueous solution and allowed to homogenization, methyl paraben, Propyl paraben, glycerin, propylene glycol were added slowly to the polymer and aqueous mixture until the gel is formed. Evaluation tests for performed for particle size, distribution, Encapsulation Efficiency , zeta potential then this preparation was incorporated in to the gel using

Hydroxypropylmethylcellulose as gelling agent. The niosomal gels were evaluated for pH, viscosity, stability, antioxidant activity. The highest Encapsulation Efficiency was obtained by the F1 formulation with the molar ratio of span: cholesterol of 3:1 i.e 77.80% and more stable at 40^0c, size: 338.3nm, distribution: 0.349nm. Suggested to add anti-oxidants to niosomal preparations to improve their stability and continue stability testing up to 12 weeks.

AN INVIVO STUDY OF HYPERICUM PERFORATUM IN A NIOSOMAL TOPICAL DRUG DELIVERY SYSTEM

They prepared a niosomal topical gel by incorporating Hypericum Perforatum to a known content of phloroglucinols, naphthodianthrones and polyphenolic compounds into an effective transdermal drug delivery system capable of entrapping both lipophilic and hydrophilic constituents in the form of niosomal gels for the treatment of wounds and scars by the reverse phase evaporation technique. Wound healing is the natural response of injured tissues, it consists of three phases they are inflammatory phase, proliferation phase and remodeling (14). Sunar et al (15) proves that the aerial parts of Hypericum perforatum possess remarkable anti inflammatory and wound healing activities by enhancing the migration of fibroblasts and collagen deposition, the compounds which present in Hypericum perforatum such as ethyl acetate fraction containing flavanoids & naphthodianthrones posses highest activity. Hypericum perforatum commonly known as st. jhons wort, a herb which has been used as an anti depressant and traditionally known as an external remedy for wounds, scars, sun burns, ulcers and hemorrhoids (10).. The Hypericum Perforatum traditional preparations contains variable components, have strong dermatological effects which favor the synergistic activity of hyperforin, hypericins and other hydrophilic components such as flavanoids and phenolic compounds (11). Niosomes are novel drug delivery system (12). They can entrap lipophilic drugs into vesicular bilayer membrane & captures hydrophilic drugs in aqueous compartments and posses a high penetrating capability than other preparations as transdermal drug delivery systems (13). Hypericum perforatum niosomal gel is prepared by reverse phase evaporation method. Firstly, by collecting the flowering tops of Hypericum perforatum allow them to dried in a vacuum oven at 40^0C. The best extraction method was determined by choosing methanol 80% & ethanol 80 % as extraction solvents both at room temperature & at 70^0C. The herb was cutted and makes it into a powder by using mixer &the powder was dispensed in to the extraction cell. The extracts were evaporated using rotary evaporator at a temperature not exceeding 40^0 C. In Reverse phase evaporation method the niosomes are prepared with different ratios of span 20,60,80. Six niosomal preparations were prepared. Then the extract was dispersed in distilled water using a sonicator. Cholesterol & span were dissolved in a mixture of chloroform & methanol stirred at 800 rpm using stirrer. The prepared extract solution was added to solvent & homogenized for 3 min. Then the suspension was then heated in a water bath for 10 minutes at 60^0C to evaporate organic solvents. Niosomal gel was prepared by dissolving the gelling agent polymer in distilled water and stirred at 270 rpm using a mechanical stirrer. Two grams of niosomal formula was added to 38 ml of distilled water and added to gel. The invivo studies are performed on mongrel dogs. The niosomal gel 1.5% sodium carboxymethylcellulose was tested in invivo studies on dogs due to its extent of drug release 78.1% after 180 min and lowers the polymer content the niosomal formulation F1Span20: cholesterol 1:1shows highest content of active constituents and 80% drug is entrapped .It results in complete re epithelization, significant reduction in the wound size as well as restoration of skin appendages and appearance of hair follicles which was a mark for the termination of the healing process. Invitro studies were performed using both 3% Hydroxyethylcellulose and 1.5% Sodium carboxymethylcellulose as polymers. The invitro drug release from both niosomal gels showed similar rates as well as extent of the drug releases after 180 min 85.0±4%, 78.8±1% for 3% Hydroxy Ethyl cellulose and 1.5%Sodium carboxymethylcellulose. The niosomal gel 1.5% sodium carboxymethylcellulose show high effects in wound treatment of 16 adult mongrel dogs compared to panthenol, assuming the synergistic activity of hyperforin's, hypericin's, flavonoids and phenolic compounds.

FORMULATION AND EVALUATION OF MORUSIN LOADED NIOSOMES FOR POTENTIATION OF ANTICANCER THERAPY.

Morusin a water-insoluble flavonoid with numerous medicinal properties, it suppresses the genes involved in the tumor progression. Due to its poor solubility of the drug, it results in low bioavailability and rapid degradation, so it has less clinical applications, to overcome this, they synthesized a niosomal formulation to improve the aqueous solubility. Morusin a prenylated flavonoid derived from the root bark of morus alba which has anti-inflammatory, anti-oxidant, antibacterial activities (8). The morusin loaded niosomes were prepared by thin layer evaporation method with slight modification. 100 mg of span 60, 20 mg of cholesterol 10 mg of drug (morusin) were dissolved in 20 ml of chloroform. The solution was allowed for stirring for 60 min after that it was kept for evaporation in a rotary evaporator for 1 hr which results in the formation of thin film. Then the film was hydrated using 20ml of distilled water to remove any residuals from the solution. After discarding the supernatant the pellet was washed with distilled water. The product morusin loaded niosomes was freeze dried & stored at 20ºC till further use. A steady & sustained drug release was observed for morusin from niosomes, along with increased release in acidic pH thus not only proposing its efficient release in acidic environment of cancer cells, but additionally reducing the spontaneous drug release in the acidic environment of cancer cells, but additionally reducing the spontaneous drug release under physiological pH of normal cells. The toxicity of morusin niosomes was tested against four cancer cell lines of different lineages depending on cell linage. According to these study cancer cells susceptibility to morusin loaded niosomes has order HT-29>MA-MB-453>PANC-1>SKOV3. They suggest that regardless of cell type of origin all cells under investigation are highly susceptible to Nanoformulation in a concentration dependent manner and predicting the utilization of this morusin niosomal formulation for multiple types of the cancer. Morusin also inhibits the survival of MDA-MB-453 which is a highly drug resistant triple negative breast cancer cell line. The results of evaluation tests are size is 479nm, Encapsulation Efficiency is 97%. Controlled & sustained release of morusin results in enhancing therapeutic efficacy was observed in cancer cell lines of four different lineages. They anticipate that morusin loaded niosomes will open new scenarios for precise delivery of morusin to cancer sites as well as lay foundation for the development of novel targeted therapies in future (9).

FABRICATION AND CHARCTERIZATION OF HERBAL DRUG LOADED NON-IONIC SURFACTANT BASED NIOSOMAL TOPICAL GEL.

They formulated an herbal drug loaded niosomes as topical gel for the treatment of bladder stones. Bladder stone is a calculus formed in the urinary bladder. The calculus is the hard mass of calcium, magnesium ammonium and uric acid salts. The stones are formed when the urine become more concentrated or due to dehydration in the body, inflammation in bladder and use of urinary catheters that cause irritation to bladder and leads to the formation of stones. Symptoms include pain in lower abdomen, burning or pain sensation at the time of urination. Initially, bladder stones can be treated of large amount of fluids, later stage by oral medications, when the size of stones are found to be large they are broke down using cytolitholapaxy or surgery is an alternative method for removal of stones (15). Niosomal topical gel has been formulated as an alternate to conventional formulations to enhance the bioavailability when compared with the oral route of administration. In novel drug delivery system, the niosomes are mostly used to enhance the permeation of the drug through the skin (6). THDC3-2615RD is a herbal drug used in the treatment of bladder stone traditionally. The herbal drug loaded niosomes was prepared by thin film hydration technique by using different ratios span 20, 60, 80 and cholesterol was dissolved in chloroform & methanol in round bottomed flask. The organic solvents were evaporated at 20^0C using Rotary evaporator. The film was found to be formed on the walls of the flask. Then the film was rehydrated with 10ml phosphate buffer 7.4 at 45^0C for 45 min in which herbal drug to be loaded & dissolved. After rehydration the niosomes were sonicated for 10 min in the bath sonicator. The niosomal gel was prepared by using Carbopol & HPMC. Carbopol increases the residence time of the drug due its hydrophilic nature. The optimized niosomal formulation was incorporated into gel base for the formulation of niosomal gel. Viscosity of the gel was carried out by using Brookfield viscometer to determine the flow behavior of the gel. The evaluation tests morphology, particle size, invitro release studies and stability studies, Entrapment efficiency was performed. Exvivo studies were performed by permeating the gel to the goat skin and result shows that 57.89% drug has been permeated at the time of 8 hrs. The optimized span 60 cholesterol/span 1:5:5 shows highest entrapment efficiency 97.12% prolonged invitro release 81.56% stability studies shows good results at 4±2ºC.Invitro release study was carried out for both gels in that niosomal gel revealed better results. Incorporating herbal drug into niosomes for a better target the drug at tissues. Gel formulation containing niosomes loaded with herbal drug shows prolonged action than the plain gel. Thus, niosomes represents a promising drug delivery for transdermal drug delivery. An increase in penetration rate has achieved to help in localized drug delivery and improves the availability of drug at their site of action which will reduce the dose and also the dose dependent side effects like irritation(7).

CONCLUSION:

To enhance therapeutic effects and bioavailability, an enormous number of attempts have been made with regard to development of drug delivery system based on herbs& their phytoconstituents with niosomes. As Herbal niosomes were prepared and optimized by various niosomal preparation methods.Niosomes considered as novel drug delivery systems, can improve the solubility and stability of natural pharmaceutical molecules. They are established to provide targeting and controlled release of natural pharmaceutical compounds.

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