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NIOSOMAL GEL OF ANTIFUNGAL DRUG KETOCONAZOLE- A REVIEW

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Kumar Kapilet al., have prepared and evaluated niosomes containing atorvastatin calcium, using different surfactants like span 20, 40, tween 20, 40, and cholesterol by modified ether ejection method. On the basis of drug content, particle size morphology, *in vitro* release and stability studies, it can be concluded that formulation NS4 (Tween 40: cholesterol, 200:100) was an optimum formulation.[41]

Latifah R et al., have prepared and evaluated curcumin niosomal gel using span 20, 60, 80 andcholesterol by reverse phase evaporation method. The result showed that Formula B (span 60:cholesterol = 7:3 in mmol ratio) has the best characters: morphology surface (multilamellarvesicles), particle size (1-5μm) and entrapment efficiency (61.22±0.004%). Formula B that formulated onto gel has an anti-inflammatory effect on peptone-induced inflammation.[42]

SunilkumarM R et al., have prepared and evaluated niosomes containing ketoconazole usingspan60 and cholesterol by modified ether injection method. Niosomes of different core: coatratio were formulated and evaluated for process yield, scanning electron microscopy, FTIR,DSC, *in vitro* drug release, kinetic studies and stability studies. It can be concluded that best-fitrelease kinetics was achieved.[43]

Sudheer P et al.,were preparedniosomes by thin film hydration technique and ether injectiontechnique consisting of various surfactants (like span 40, 60, tween 40, 60) and cholesterol, at different specified ratios. Formulations prepared by thin film hydration technique, using drug, tween 40 and cholesterol in a ratio of 1:1:1 resulted in better entrapment efficiency and vesicular size in comparison to ether injection method. The niosomal formulations werecharacterised for vesicle size distribution, SEM and zeta potential. The best formulation (F16) was selected on the basis of drug entrapment efficiency of 83.63 ± 0.11% and *in vitro* diffusion profile. A comparative *ex vivo* permeation study of niosomal gel against marketed gel, 2.5% w/w gel on excised rat abdominal skin model indicateda two-fold increase in permeation in comparison to marketed gel and a threefold increase in permeation in comparison to 2.5% w/w ketoprofen gel formula.[44]

Sidramappa B S et al., have developed niosomal gel formulation of clotrimazole to increase retention time in the dermis layer through controlled release of the drug by thin film hydration method using span-40 and cholesterol. The niosomal dispersion was evaluated for vesicle size, surface morphology, percent entrapment efficiency and *in vitro* drug release. The results suggested that encapsulating clotrimazoleniosomes would provide better patient compliance by achieving prolonged release of the drug to the dermis with improved efficacy.[45]

Chawan M *et al.*, Have formulated niosomal dispersions by ether injection method with different molar ratios of surfactant and cholesterol, by changing the surfactant concentration but keeping the cholesterol concentration constant. The surfactant used was Span 60 and the five batches of niosomal preparations were prepared in the ratios 1:1:1, 1.5:1:1, 2:1:1, 2.5:1:1 and 3:1:1 (surfactant: cholesterol: drug). Furthermore, the release profile, entrapment efficiency, size distribution and stability of these niosomes under various temperatures were studied. Inverted microscopic evaluation showed that formed by direct hydration are very heterogeneous and wereboth unilamellar and multilamellar in their structures.[46]

Saraf S A *et al.*, were prepared niosomal formulation for the delivery of isoniazid to achieve effective treatment of tuberculosis. worked for their particle size, poly dispersity index (PI) and zeta potential as well as by scanning electron microscopy, in- vitro drug release,

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and cellular uptake studies on the niosomes by macrophage J744A were undertaken, Cellular uptake of the drug-loaded niosomes by macrophage cells was as high as 61.8 %, a level that is capable of achieving effective treatment of tuberculosis. The isoniazid niosomes developed are capable of reducing drug dose and toxicity as well as dosing frequency which should bring about improved patient compliance.[47]

Kapoor A *et al.,* Have formulated niosomes by reverse phase evaporation method using sorbitanesters (Span 20, 40, 60, and 80) and cholesterol in different molar ratio and acyclovir as the model drug. Prepared niosome were characterized for their *in-vitro* drug release efficiency, the results indicated that more sustained release pattern can be obtained by incorporating the drug. Incurrent study, release of acyclovir entrapped in large unilamellar vesicles composed of surfactant/cholesterol (90%surfactant/10%cholesterol), it appears that acyclovir efflux form niosomes is a process containing slower release phase achieved within 2-4 hours.[48]

Y Prem Kumar *et al.,* Were formulated and evaluated of econazol niosome by thin film hydration technique by varying the cholesterol and surfactant ratios as 1:1, 1:2, 1:3, 1:4, formulation was evaluated for drug release for percentage of drug entrapment and for their cumulative drug represent experiments, It may be concluded that formulation A4 containing 1:4 ratio was showing high percentage of entrapment and desired sustained release of econazol. [49]

Navya M N *et al*., Were prepared span-60 flutamide niosome were evaluated for their vesicle shape, entrapment efficiency, drug content, compatibility studies and *in- vitro* drug release. The *in- vitro* release studies indicated that all the formulation exhibits retarded release for 24 hours and its release mechanism was followed by Higuchi order kinetics. The study demonstrated the successful preparation of flutamide niosomes and their evaluation. Formulation F1 showed high entrapment efficiency (92.12%), particle size (4.40 μm) and drug release (74.50%) over 24 hrs. Hence it was considered to be good niosomal formulation with greater bioavailability.[50]

Vilegave K *et al.,*Were worked on niosomes stability in biological environment by hand shaken method using flurosant markers like 5-6-Carboxyfluroscein and drug release rate was evaluated in biolgical media that is (serum & plasma) as a function of surfectant composition and in the presence or absence of cholesterol. Surfactant charge measurment is done by zeta potential as a function of pH, gel electrophoresis and immunoblotting were used to know the compatability study between biological fluid componant and prepared vesicles. It was found that the entire vesicle carries negative charge & rapidly bound to the plasma protein results, as reported for liposomes, in the formation of large unilamellar vesicles, with good entrapment efficiencies and greater stability. They have also investigated the uptake & degradation of niosomes in a living unicellular, eukaryotic micro-oraganism.[51]

Syed M A *et al.,* Were worked on sustain release of ophthalmic niosomal in-situ gel of norfloxacin which increase the drug residence time in the eye, by using Carbopol940 – a pH sensitive gelling agent, useful in the treatment of bacterial conjunctivitis, to increase the ocular residence time of drug. The pH of the formulations was found to be satisfactory and was in the range of 6.2-6.8 were liquid at room temperature when compared with all the formulations, from this we found that entrapment efficiency , size and shape of drug, and gelling capacity. For the drug to be released in the medium, it has to pass through the vesicle wall and then through the hydrogel matrix. Initially, the un-entrapped drug was released from the in-situ gel which can serve as the initial loading dose. Thereafter, the niosomes can release drug in a sustained manner making the formulation suitable for once a day dosing.[52]

M. R. Sunilkumar *et al.* Were prepared ketoconazole loaded noisomes by modified ether injection method by using of span60 with cholesterol. Niosomes of different core:coat ratio were formulated and evaluated for process yield, scanning electron microscopy, FTIR, DSC, in vitro drug release, kinetic studies and stability studies. The prepared niosomes were white, freeflowing, spherical in shape. The infrared spectra and differential scanning calorimetry thermographs showed stable character of ketoconazole in the niosomes containing drug and revealed the absence of drug polymer interactions. The *in- vitro* release behavior from all the drug loaded batches were found to follow first order and provided sustained release over a periodof 24 h and no appreciable difference was observed in the extent of degradation of product during 90 days in which niosomes were stored at various temperatures. The best-fit release kinetics was achieved.[53]

Yadav S *et al.,* Have formulated and evaluated topical gel containing ketoconazole for treatment of fungal infection of skin, It was encapsulated in liposomes for topical application. ketoconazoleliposomes were prepared by thin film hydration technique using soya lecithin, cholesterol and drug in different weight ratios. The prepared liposomes were characterized for entrapmentefficiency, *in-vitro* drug release and viscosity release kinetic. The present study showed that F2 formulation gives best percentage yield, drug content, entrapment efficiency and shows best dissolution release. So it was conclude that F2 formulation should be a better candidate for liposome gel with best . [54]

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Prince S *et al*., Were worked on naproxen loaded niosomes, prepared naproxim niosomalformulation were further characterized from there particles size and shape, entrapment efficiency,in-vitro release, skin irritation. Solubility of naproxen in different solvents was performed, the study indicates the affinity of naproxen toward non-aqueous solvents was better, and insoluble indistilled water, % moisture content and loss on drying was found to be 0.704 and 0.70 respectively.[55]

Benipal G *at el*., Have formulated proniosomal gel of ketoconazole by using different non-ionic surfactants and evaluated for vesicle size, entrapment efficiency. The entrapment efficiency of drug in optimized formulation (F3) containing Span 60 is high (94.93%), the extent of drug permeation through the membrane was also quite high (93.52%) after 24 hrs. The above results indicate that the proniosomal gel of KTZ could be formulated for sustained release usingoptimum concentration of cholesterol, lipid and suitable surfactant to deliver a desired concentration of drug at site of action. From the stability study it can be concluded that 5 ± 3°Cis the most suitable temperature for the storage of the proniosomal gel formulation.[56]

Indira S *et al.,* Were formulated nasal niosome in situ gels of loratadine using by thin film hydration technique. It has higher entrapment efficiency (94.87%) and *in-vitro* drug release (59.90%) . Microscopic evaluation showed that most of the vesicles were spherical in shape, the diameter (nm) of niosomes in the range of 200 to 1000 nm and the average particle size was 266nm. The zeta potential of the niosomes was determined using Zetasizer and the value of the was found to be -77 mv as that niosomes were stable.[57]

Rokade VS *et al.,* Have formulated antibacterial ciprofloxacin cream by thin film hydration technique using rotary vacuum evaporator and were incorporated into cream base. The formulation was optimized by changing the ratio of Span 60 and lipotin based on maximum entrapment efficiency and drug retention using ex-vivo drug diffusion study. Techniques such as ultra turrax and high pressure homogenization (HPH) were carried out to obtain size reduction and narrow size distribution lower PDI. The results indicated satisfactory size reduction and low PDI but affected the entrapment efficiency adversely which could be due to vesicle rupturing at high pressure and speed.[58]

Mohsinet *et al*., Were prepared silibinin containing nanoniosomes in T47D human breast by reverse phase evaporation method. Mixture of span 20, silibinin, PEG-2000 and cholesterol in chloroform and methanol solvent (1:2 v/v) was used for preparation of niosome. Mean size, size distribution and zeta potential of niosomes were measured and then nano particles underwent scanning electron microscopy**.** In there research, niosomal silibinin was conducted to optimize and assess the toxic effects on breast cancer cell. The research showed an increase in cytotoxic effects of silibinin loaded on the niosomes compared with free form of silibinin. However, nanoniosome synthesis techniques have proved beneficial in improving of drug in the target site.[59]

Gyati SA *et al.,* Have worked to formulate etodolac topical gel and was characterized with respect to its various parameters such as pH, viscosity, spreadability, ex- vivo study, and in- vivopotential permeation. The study suggested that topical niosomal gel formulation provide sustained and prolonged delivery of drug. Developed niosomal formulations were characterized with respect to particle size, shape, entrapment efficiency, and *in-vitro* drug release profile. Morphology of niosomal formulations were determined by optical microscopy, from this it was clearly observed that niosomes are spherical in shape, and mean particle size of the niosomal formulation was found to be 2 µm to 4µm.[60]

RajendranV et al., have prepared and evaluated sertraline HCl niosomes by ether injection method using surfactants such as span 40(A), span 60(B) and span 80(C) along with cholesterol at a ratio of 1:1. Four different concentrations (200:200(Aa), 250:250(Ab), 300:300(Ac) &350:350(Ad)) of surfactant and cholesterol were used for each surfactant. The optimized formulation was subjected to physical stability studies. Higher encapsulation efficiency of 53.71%±3.2%, 51.18%±2.5% and 51.92%±2.7% were obtained for Ad, Bb and Bc respectively. A maximum sertraline HCl release of 70%±2.6% was obtained for Ad which showed a permeation of 2.71%±0.157% across mouse skin. A calculated 50.2%±0.9% of sertraline HCl was assumed to get accumulated in the skin layers and the niosomes were physically stable. Sertraline HCl niosome showed a slow and prolonged release of sertraline HCl through the mouse skin and thus holds promise for transdermal delivery.[61]

Sonia Tomaret al.,was studied the preformulation parameters of azithromycin and prednisolone for niosomal gel. The objective of the study was made to develop sustained release gel containing azithromycin and niosomal vesicles of prednisolone using carbopol as a polymer which will control the release of drug, increasing the bioavailability of the drug and thusdecreasing the dosing frequency of the drug. The preformulation studies were carried out for identification (physical appearance, melting point, and UV spectrophotometer), solubility profile,TLC, FTIR, compatibility studies, simultaneous estimation.[62]

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Jaiswal P A et al., have prepared niosomal gel of diclofenac sodium using span 20, 60 and span 20: 60 combination ratio by thin film hydration method and was evaluated using physical parameters, p^H determination, content uniformity, extrudability, spreadability, degree of deformability testing. Niosomes prepared with span 60 provided a higher permeation across the skin than that of span 20 and span20: 60 combination ratios. Changes in the cholesterol content affect the encapsulation efficiency and permeation of gel. The encapsulation (%) of niosomes with span 60 surfactant showed a very high value of ~100% due to its low surface energy decreases the size of vesicle and drug permeation increases.[62]

Kumar Kapilet al., have prepared and evaluated niosomes containing atorvastatin calcium, using different surfactants like span 20, 40, tween 20, 40, and cholesterol by modified ether ejection method. On the basis of drug content, particle size morphology, *in vitro* release and stability studies, it can be concluded that formulation NS4 (Tween 40: cholesterol, 200:100) was an optimum formulation.[63]

Dhole V M et al., have prepared and evaluated niosomal cream using span 80, tween 80, soya lecithin, and cholesterol by rotary evaporation hydration method. Octopirox loaded batches of niosome were prepared and evaluated for size, shape and Entrapment efficiency. The results showed that span 80 having higher entrapment efficiency than tween 80.Evaluation of cream containing niosome was carried out for viscosity, measurement of pH, spreadability etc. It can be concluded that the formulation evaluated for the drug release of the optimized batch i.e. V- using o/w cream base, it was concluded that the drug release rate increases with its increasing concentration.[64]

Shirsand S B et al., have prepared niosomes containing ciclopiroxolamine by ether injection method using non-ionic surfactants (span 40, 60) and cholesterol at different concentrations. The prepared formulations were evaluated for optical microscopy, entrapment efficiency, drug content, *in vitro* release study and stability studies. CNS61(containing span 60) showed higher entrapment efficiency compare to span 40 by these formulation CNS61 was found to be the best formulation having vesicle size 8.81µm, entrapment efficiency of 71.45±0.44 and drug release of55.345±1.009 at the end of 24 hr. The study indicated that all the formulations prepared by ether injection method using non-ionic surfactant showed sustain drug release rate for 24 hrs. Slope values of peppas log-log plots are between0.634 to 0.763 suggested that the drug release by non- fickian release mechanism.[65]

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