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"FORMULATION AND EVALUATION OF ANTIFUNGAL NEOSOMES OF KETOCONAZOLE"

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Abstract-Formulation of niosome of ketoconazole was prepare by hand shaking method (thin film hydration technique) and then converting into gel by adding gelling agent carbopol 934. Four formulations were prepared and characterized by different parameter like entrappment efficiency, drug content, morphology, pH, percentage yield, *in- vitro* release and stability studies.

In study all formulations shows good results but on the basis of drug content ,percentage yield,in vitro release and stability studies F1 formulation found the best.

Conclusion- Niosomes can be used for further formulation development like ointment creams or gel for topical use to treat fungal infections.

INTRODUCTION

Novel drug delivery system

In the past few decades, considerable attention has been focused on the development of novel drug delivery system (NDDS). The NDDS should ideally fulfill two prerequisites. Firstly, it should deliver the drug at a rate directed by the needs of the body, over the period of treatment. Secondly, it should channel the active entity to the site of action. Conventional dosage forms including prolonged release dosage forms are unable to meet none of these. At present, no available drug delivery system behaves ideally, but sincere attempts have been made to achieve them through various novel approaches in

drug delivery.[1-4]

Merits of novel drug delivery system

- Targeting of the drug molecule towards the tissue (or organ reduces the toxicity to the normal tissues.
- Improved patient compliance resulting from the reduction in the frequency ofdoses required to maintain the desired therapeutic response.
- Devoid of gastrointestinal tract degradation and first pass metabolism.[8-10]

Limitations of novel drug delivery system

To control the frequency and rate of drug delivery at the pharmacological receptor, Reduction in the drug dose and side effects., Exclusive drug delivery to the specific cells or diseased site in the body.[11]

FORMULATION AND EVALUATION OF KETOCONAZOLE NIOSOMES

Ketoconazole loaded niosomes were prepared by Thin film hydration technique.Accurately weighed quantity of cholesterol and surfactant were dissolved in chloroform methanol mixture ratio (2:1v/v) in a 100 ml volumetric flask. The weighed quantity of drug and dicetyl phosphate was added to the solvent mixture. The solvent mixture was removed from liquid phase using rotary evaporator at 60°C to obtain a thin film on the wall of the flask at a rotation speed of 150 rpm. The complete removal of solvent can be ensured by applying vaccum. The dry lipid film was hydrated with 5 ml phosphate buffer saline of Ph 7.4 at a temperature of 60±2°C for a period of 2 hour until the formation of niosomes. All thebatches were subjected to sonication process for 2 min using probe sonicator.[12]

COMPOSITION OF KETOCONAZOLE NIOSOMES

EVALUATION OF KETOCONAZOLE NIOSOMES

Removal of unentrapped drug from niosomes[13-14]

The unentrapped drug from niosomal formulation was separated by centrifugation method. The niosomal suspension was taken in centrifuge tube. The formulation was centrifuged at 15,000 rpm for 30 min using cooling centrifuge and temperature was maintained at 5°c. The supernatant was separated. Supernatant contained unentrapped drug and pellet contained drug encapsulated vesicles. The pellet was resuspended in phosphate buffer saline pH 7.4 to obtain a niosomal suspension free from unentrapped drug.

Encapsulation efficiency

Drug entrapped vesicles were separated from unentrapped drug by centrifugation method.

0.5 ml of zidovudine loaded niosome preparation was added with 0.5 ml of 10% triton X 100 and mixed well then incubated for 1 hour. The triton X 100 was added to lyse the vesicles inorder to release the encapsulated zidovudine. The solution was diluted with phosphate buffer saline pH 7.4 and filtered through whatmann filter paper. The filtrate was measured spectrophotometrically at 267 nm using phosphate buffer saline pH 7.4 and triton X 100 mixture as blank.

Zeta potential

The zeta potential of optimized niosomal formulation was measured using Malvern zeta potential analyser.

Scanning electron microscopy

The optimized formulation was morphologically characterized by scanning electron microscopy (SEM). The sample for SEM analysis was mounted in the specimen stub using an adhesive small sample was mounted directly in scotsch double adhesive tape. The samplewas analysed in hitachi scanning electrom microscope operated at 15 kv and photographwas taken.

Morphology analysis:

Prepared liposomes for all the formulations were viewed under for observing the vesicle formation and discreteness of dispersed vesicles. A slide was prepared by placing over it and this slide was viewed under optical microscope at 40x magnification photographs were takento prepared slides using digital camera.[15]

In-vitro drug release study:

The *in vitro* release for all formulated ketoconazole neosomes were carried out for 8 hours using in phosphate buffer pH 6.8. The studies were carried in USP dissolution apparatus at $37^0C \pm 0.5^0C$ and 50 rpm speed.900 ml of phosphate buffer pH 6.8 was used as a dissolution medium.1ml of samples were withdrawn at every 30 mins upto 480 mins and make upto 10 ml with pH 6.8 and analyzed for ketoconazole content at 294nm with pH 6.8 as blank using UV-Spectrophotometer[16]

Percentage yield of niosomes

The prepared neosomes were collected and weighed. The measured weight was divided by the total amount of drug and excipients which were used for the preparation of neosomes[17]

pH measurement

The obvious pH of niosomal formulation was measured by digital pH meter intriplicate manner[18]

Determination of drug content

Drug entrapped multilamellar niosomes (100 mg) were suspended in 100 ml solution of chloroform: methanol (2:1). The resultant dispersion was kept for 20 min for complete mixing with continuous agitation and filtered through a 0.45 µm membrane filter. The drug content was determined spectrophotometrically at 294 nm using a regression equation derived from the standard graph. Results were based on triplicate determination[19]

Stability studies

The behaviour of niosomes to retain the drug was studied by storing the niosomes at two different temperature conditions,i.e., 4^0C(refrigerator RF),$25^0C \pm 2^0C$ for a period of one month.The niosomes preparations were kept in sealed vials. At 30 th day the samples were analyzed for the drug content following the same method described in % drug encapsulating efficiency, Physical appearance and also the niosomes were studied for their morphology[20]

RESULT AND DISCUSSION

Drug entrappment efficiency

The drug entrappment efficiency was carried out for all four formulations.

In-vitro drug release studies:

The *In-vitro* drug release studies of all the formulations of niosomes were carried out in

phosphate buffer saline pH 7.4 solution. It was observed that the ratio of soyalecithin,drug and cholestrol influences the drug release pattern

Percentage Yield of Liposomes:

Percentage practical yield of different formulations was determined by weighing. The percentage yield of different formulation was in the range of 77 to 94%. The percentage yield of formulation F1 is more than F2 and F4 is more than F3.

pH measurement:

The pH of all four formulations were determined by digital pH meter. pH of all the formulationswas obtained in the range of 5.75 to 5.99

Determination of drug content

The drug content of all four formulations was in the range of 85 to 92%

Stability studies:

The stability studies of liposomal prepations carried out after one month at two different tempearature conditions,i.e., 4^0C(refrigerator RF),25^0C± 2^0C(room temperature).

SUMMARY AND CONCLUSION

In the current research study, formulation of niosome of ketoconazole was prepare by hand shaking method (thin film hydration technique) and then converting into gel by adding gelling agent carbopol 934. Four formulations were prepared and characterized by different parameter like entrappment efficiency, drug content, morphology, pH, percentage yield, *in- vitro* release and stability studies.

In study all formulations shows good results but on the basis of drug content ,percentage yield,in vitro release and stability studies F1 formulation found the best.

So by this study this is concluded that we can use this niosomes for further formulation development like ointment creams or gel for topical use to treat fungal infections.

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