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Niosomal Delivery of Tenoxicam

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The new trends in the development of drug delivery systems are based on the application of the concepts and techniques of targeting drugs to specific sites in the body using various carriers and vehicles as drug delivery devices[1,2]. This study describes the encapsulation of Tenoxicam in niosomes and investigates the influence of the varying proportion of surfactant, cholesterol and dicetyl phosphate on the morphology, particle size distribution, entrapment efficiency and in-vitro drug release of niosomes.

TENOXICAM was obtained from Ranbaxy Laboratories Ltd., New Delhi, Dicetyl phosphate, Sigma Chem. Co., St. Louis USA, Cholesterol from S.D. Fine Chem. Ltd., Mumbai Carrageenan, Indian Gum Industries Ltd. and Cellophane membrane from Kesavarm Rayon India.

The niosomes were prepared by hand shaking method as described by Baillie et al[3], and Azmin et al[4]. Different batches of niosomes were prepared using accurately weighed quantities of the Span 60/cholesterol/dicetyl phosphate respectively as molar mixture viz. B_1 (50:50), B_2 (60:40), B_3 (70:30), B_4 (80:20), B_5 (90:10), B_6 (47.5:47.5:5), B_7 (60:35:5), B_8 (Span 60 only 100 μmol), B_9 (Span 60 only 200 μmol).

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The lipid ingredients were dissolved in 10-15 ml of diethyl ether and transferred to a 50 ml round bottomed flask. The ether was removed at room temperature under reduced pressure on a rotary film evaporator (Buchi type) to form a thin dry film on the inner wall of the flask. The dried surfactant film was hydrated with 5 ml of aqueous phase at 60° be gentle agitation for one hour to obtain a milky dispersion of niosomes.

The aqueous phase used for film hydration was either 5 ml drug solution, (2 mg/ml of Tenoxicam) or 5 ml buffer solution to give drug loaded or empty niosomes respectively. All the batches of niosomes were triplicated.

The niosomes were examined under the optical microscope. The major proportion of niosomes were

Table1: Invitro Stability of Tenoxicam in Niosomes

Time (hrs)	Percent Drug Retained in Niosomes Containing				
	Surfactant: Cholesterol:: 50:50	Surfactant: Cholesterol:: 60:40	Surfactant: Cholesterol:: 70:30	Surfactant:Cholesterol:: Dicetyl phosphate 47.5:47.5:5	only Surfactant
1	72.18	69.28	61.01	48.63	71.14
2	69.91	66.19	57.76	41.32	69.54
3	68.63	64.53	56.12	38.51	68.84
4	68.06	65.04	55.68	34.24	67.46
5	67.27	63.24	55.25	30.45	67.24
6	67.14	63.04	54.22	31.11	67.19
7	67.07	62.67	54.42	31.00	67.56
8	66.00	62.33	54.03	31.00	67.56
24	66.83	61.99	53.75	31.00	67.65

spherical in shape. The multilamellar structure of the vesicles can be seen in the **Photomicrograph** (Fig:1). It has been reported that multiamellar vesicles are more appropriate for local therapy and particles of 0.5 - 5 μm are retained more effectively in joint cavity[5,6]. Hence niosomes with an optimum range i.e. Batches B_1, B_2, B_3, B_6 and B_8 were selected for further studies (Fig. 2). The unentrapped drug was removed from the niosomal dispersion by gel chromatography[7,8]. As this technique caused dilution of the dispersion, the unentrapped drug was removed by passing it through a sintered funnel under vacuum. Repeated washings with alkaline buffer pH 8.4 were given. The free drug was removed after 8 - 10 changes of the buffer. The washings were complete when no Tenoxicam was detectable in the recipient solution. The next step involved was the lysis of the niosomes with acetone solution. The amount of Tenoxicam dissolved in the buffer was determined spectrophotometrically by measuring absorbance at 369.4 nm against buffer pH 8.4 as blank. Tenoxicam concentration was calculated as the ratio of the absorbance of sample versus the slope of the calibration curve. Since the initial amount of Tenoxicam used for the preparation of niosomes was 20 mg, by subtracting the amount of Tenoxicam obtained in the washings after lysis would yield the amount of drug in the niosomes. The entrapment efficiency of the different batches of niosomes ranged from 11.423% to 23.766%. Highest entrapment efficiency was obtained in niosomes prepared using surfactant alone.

In-vitro release characteristics of Tenoxicam from niosomes were studied using a pretreated cellulose membrane[9]. The cellophane membrane was pretreated by boiling in distilled water for 15 minutes and was tied firmly on the end of a hollow glass tube fitted with a wire mesh. A niosomal suspension was placed inside the tube and it was suspended in phosphate buffered saline solution pH 7.4 with constant stirring of the external phase. The receiver solution was completely withdrawn and replaced with fresh phosphate buffered saline of pH 7.4 at each scheduled time. This was repeated till all the unentrapped drug was removed from the niosomes. Agitation was provided by a magnetic stirrer and the temperature was maintained at 37°. 5 ml samples
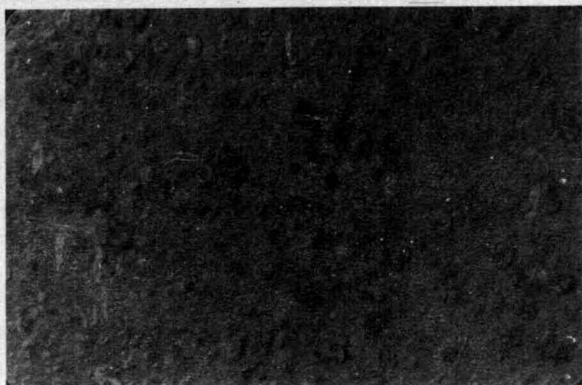
Fig. 1: Niosomes prepared using Surfactant : Cholesterol : DCP : 47.5 : 47.5 : 5

were removed at fixed time intervals and the volume compensated by adding a fresh quantity of equal volume of phosphate buffered saline into the beaker. The released drug was measured spectrophotometrically. Release occurred in two distinct phases, an initial burst release which lasted for 2-4 h., followed by a sustained but reduced release which was maintained for atleast 24 h. This biphasic release pattern might be due to size heterogenicity of the vesicles. The incorporation of cholesterol and dicetyl phosphate had the effect of decreasing the release. These lipids are retained within the niosomal membranes and decrease the diffusion of Tenoxicam through the membrane (Fig: 3).

For testing **in-vitro** stability, blood samples were withdrawn from the retinovulvar plexus of the eye of Albino rats using hematocrit capillaries. The blood was kept undisturbed for some time and the serum separated by centrifugation at 3000 rpm for 10 min. The **in-vitro** stability of niosomes was determined by incubating a 0.5 ml aliquot of the preparation in 0.5 ml of serum and determining the amount of drug leaked at various time intervals.

From the **in-vitro** stability studies it appears that the presence of a sufficient amount of cholesterol in niosomes is essential for the maintenance of their stability in the presence of serum, **in-vitro**. Only

Size Distribution Of Niosomes Prepared Using Surfactant : Cholesterol : Dicetyl Phosphate : 47.5 : 47.5 : 5
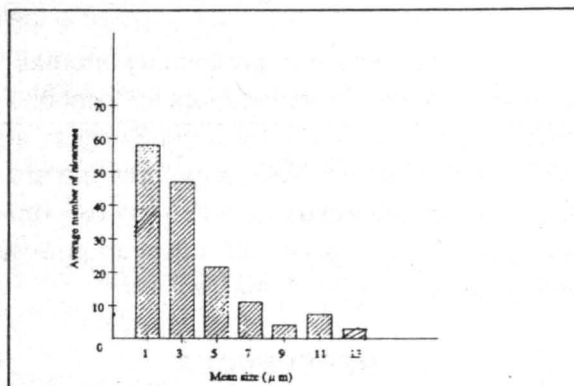

Fig. 2

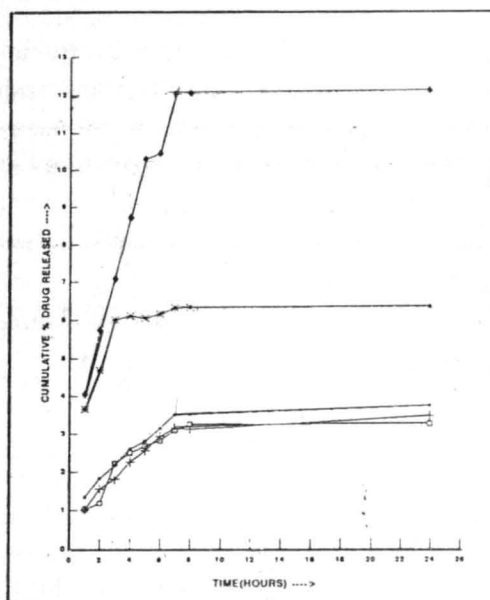**INVITRO RELEASE PROFILE OF TENOXICAM IN PBS (pH 7.4)**

Fig. 3

Surfactant : Cholesterol: : 50:50
Surfactant: Cholestrerol: : 60:40
Surfactant: Cholesterol: : 70:30
Surfactant: Cholesterol: DCP::47.5:47.5:5
Only Surfactant

31.01% of Tenoxicam was retained in niosomes prepared using surfactant alone while niosomes prepared using surfactant - cholesterol mixtures retained 53.8% - 67.0% of the drug (Table I).

It appears from our preliminary studies that niosomes may be suitable carriers for local and oral therapy. By varying the vesicle composition, stable vesicles with optimum size range, entrapment efficiency and drug release properties can be prepared resulting in a formulation with optimum pharmaco-kinetic and therapeutic characteristics.

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Regression Analysis of Aqueous Solubility Data - Polycyclic aromatic hydrocarbons and Steroids

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The aqueous solubility data of polycyclic aromatic hydrocarbons and steroids was regressed to predict the level of solubility. Hildebrand - Scatchard equation format was used in the regression model. The correlations were fairly high (≈86%) for hydrocarbon series and appreciable for steroids (≈ 62%). A comparison of coefficients indicate that the solubility of steroids are twice that of the predictions obtained for polycyclic aromatic hydrocarbons. The functional groups on the skeleton structure might have interacted with water strongly and enhanced its solubility.

AQUEOUS solubility has long been identified as a key factor in the design of solution dosage forms. Water is generally recognised as a highly irregular solvent, and therefore, aqueous solution do not comply with regular solution theory.[1] However, if the solute is sufficiently nonpolar or inert, the aque-

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