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Research Article

DEVELOPMENT AND EVALUATION OF NIOSOMAL DELIVERY SYSTEM FOR ACECLOFENAC

Mohamed Hassan Dehghan*[a], Mohammed Asif Hussain [b]

[a]Department of Pharmaceutics, Y.B. Chavan College of Pharmacy, Aurangabad, Maharashtra, India.

[b] Department of Pharmaceutics, Luqman College of Pharmacy, old jewargi road, Gulbarga, Karnataka, India.

E mail: asifhussainp@yahoo.com

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ABSTRACT

Aceclofenac is a NSAID with a half life of 4-5 hrs. It is used in the management of osteoarthritis, rheumatoid arthritis and ankylozing spondylitis. The current investigation aimed to evaluate the novel potential of ether injection technique to produce niosomes bearing aceclofenac water insoluble analgesic and antipyretic drug, with sustained release behavior and decrease the GI disturbances as it will be encapsulated in vesicles. On formulation with above technique spherical niosomes were obtained. The prepared niosomes were characterized by vesicle diameter, entrapment efficiency; in-vitro drug release and Fourier transform infra red spectroscopy (FT-IR).

The drug loaded niosomes showed 60.80% to 84.44% entrapment efficiency. The mean vesicle diameter was found to be varied by changing different surfactant concentration. The *in-vitro* release profile could be altered significantly by changing span concentration to give a sustained release of drug from the niosomes. The microscopic study indicated that niosomes were spherical in shape. FT-IR study confirmed the drug stability in the niosomes. It was also observed that span20, span80, cholesterol and aceclofenac underwent physical interaction such as hydrogen bonding or overlapping. The maximum in-vitro release of aceclofenac (BatchA) i.e A_5 99.97% in 24 hrs was observed for preparation of niosomes containing aceclofenac (120mg) and span 20(120mg) by ether injection method. For Batch B the maximum in-vitro release of aceclofenac was 90.13% in 24 hrs observed for aceclofenac (120mg) and span 80 (140mg) by ether injection method. The in-vitro drug release mechanism shown

was of three types matrix diffusion type, zero order and first order type. Thus ether injection technique can be successfully used to prepare niosomes of aceclofenac, a water insoluble drug with high entrapment efficiency and prolonged release behavior.

KEY WORDS: Aceclofenac, Ether Injection technique, Niosomes, Vesicular diameter, Entrapment efficiency & In-vitro drug release

INTRODUCTION

The goal of any drug delivery system is to provide a therapeutic amount of drug to the Proper site in the body to achieve promptly and then to maintain the desired drug concentration. That is, the drug delivery system should deliver drug at a rate dictated by the needs of the body over a specified period of treatment. This idealized objective points to the two aspects most important to drug delivery namely spatial placement and temporal delivery of a drug. Spatial Placement relates to targeting of drug to a specific organ or tissue, while temporal delivery refers to controlling the rate of drug delivery to the target tissue. An appropriately designed controlled release drug-delivery system can be a major advance towards solving these two problems[1]. In this work niosomes are being used to attain above two aspects. Niosomes are unilamellar or multi-lamellar vesicles, wherein an aqueous solution is enclosed by a bilayer structure made up of non-ionic surfactant with or without cholesterol and charge inducers, which can accommodate both hydrophobic and hydrophilic drug either in aqueous or bilayer region of vesicles[2].

Aceclofenac is a non-steroidal anti inflammatory analgesic agent. After oral administration, aceclofenac is rapidly & completely absorbed as unchanged drug. Peak plasma concentrations are reached approximately 1.25 to 3.00 hrs following ingestion. Aceclofenac is highly Protein bound > 99% and two third of the administered dose is excreted via the urine, mainly as hydroxy metabolite[3].Prolonged use of the drug is associated with gastro intestinal disturbances such as GI discomfort, nausea, diarrhea and peptic ulceration[4].

The aim of the present study was to compare the efficiency of two batches (span20, Span80) by Ether injection method for sustained release of drug, reduce GI disturbances and evaluation of batches of niosomes

containing aceclofenac for following parameters (a) vesicular diameter (b) Entrapment efficiency (c) in-vitro drug release.

Materials and Methods

Materials: Aceclofenac was obtained as a gift sample from Suyash Laboratories, MIDC, and Tarapur. Span 20, Span 80, Cholesterol was obtained from Loba Chemie Pvt. Ltd., Mumbai. Diethyl ether, Sodium hydroxide, Potassium dihydrogen orthophosphate was Supplied from Sd Fine Chemicals Ltd., Mumbai.

Methods:

Preparation of Aceclofenac Loaded Niosomes with Span 20, Cholesterol:

Ether Injection Method

Aceclofenac loaded niosomes using span 20, cholesterol were prepared using 3^2 factorial design with span 20 and aceclofenac as variables and maintaining the amount of cholesterol (100 mg) as constant. The method used for the preparation of these niosomes was ether injection method[5]. Niosomes containing aceclofenac were prepared by weighing calculated amount of span 20 and cholesterol in a 50 ml beaker. The mixture was dissolved in 10 ml of diethyl ether and the solution was drawn into a syringe. Then the solution was slowly injected at a rate of 1 ml/ min into a beaker containing calculated amount of drug in 20 ml of phosphate buffer pH 7.4 and was stirred simultaneously with a magnetic stirrer. The temperature maintained during the injection was 60ºC.

Table: 1 Factor & Levels in the Design of Aceclofenac Loaded Niosomes with Span 20 and Cholesterol

Independent variables	LEVELS		
	(–1) Lower	(0) Middle	(+1) Upper
Span 20 (X_1) mg	100	120	140
Drug (X_2) mg	100	120	140

(Amount of cholesterol (100 mg) was maintained constant in all the preparations).

Table: 2 Experimental Batches for Factorial Design:

Batch-A

Run No	X_1	X_2
1	–1	–1
2	–1	0
3	–1	+1
4	0	–1
5	0	0
6	0	+1
7	+1	–1
8	+1	0
9	+1	+1

Preparation of Aceclofenac Loaded Niosomes with Span 80, Cholesterol:

Ether Injection Method

These formulations were prepared in the same manner as the above batch by using span 80 instead of span 20.

EVALUATION:

Vesicular diameter: It was carried out using an optical microscope (Olympus, Japan) with a calibrated eyepiece micrometer[5]. About 25 niosomes were measured individually from each formulation, average was taken add their size range and mean diameter were calculated.

Entrapment efficiency: Separation of unentrapped drug was done by suspending the niosomes into a dialysis tube to which a sigma dialysis membrane was securely attached to one side[6]. The dialysis tube was suspended in 75 ml. pH 7.4 phosphate buffer, which was stirred on a magnetic stirrer. The unentrapped drug was separated from the niosome suspension into the medium through semi permeable membrane. At every half an hour interval 75 ml of

the whole medium was replaced with fresh medium (for about 4-5 hours) till the absorbance reached a constant reading.

Fourier – Transform Infrared Spectroscopy (FT – IR)

The drug and other excipient interactions were investigated by FT – IR spectroscopy. The cholesterol, span20, span80 and aceclofenac loaded niosomes using shimadzu FT-IR – 72425 models. The scanning range was from 4000cm^{-1} to 400cm^{-1}

***In Vitro* Drug Release:**

The niosomal suspension containing known amount of aceclofenac was transferred to dialysis tube[5] and subjected to dialysis with the dialysis tube immersed in a receptor compartment containing phosphate buffered saline, pH 7.4 (75 ml), which was under constant magnetic stirring. Samples (5 ml) were withdrawn at predetermined time intervals and replaced by fresh medium and drug content was determined spectrophotometrically at 275nm.

Table: 3 Vesicular diameter and Entrapment efficiency of Aceclofenac Loaded Niosome containing Span 20

Run No.	Formulation Code	Vesicular diameter (µm)	Entrapment efficiency (%)
1	A_1	10.58	69.827
2	A_2	10.90	84.447
3	A_3	11.20	81.516
4	A_4	10.36	79.162
5	A_5	10.52	82.628
6	A_6	10.80	81.734
7	A_7	10.20	66.220
8	A_8	10.45	78.663
9	A_9	10.72	70.397

Table: 4 Average Vesicular diameter of Aceclofenac loaded Niosomes Containing Span 20

X_1	**-1**	0	+ 1
Avg. Vesicular Diameter	10.98 (µm)	10.56 (µm)	10.45 (µm)

Table: 5 Average Entrapment efficiency of Aceclofenac Niosomes containing Span 20

X1	**-1**	0	+1
Avg. Entrapment efficiency (%)	78.59	81.17	71.76

Table: 6 Vesicular diameter of Aceclofenac loaded Niosomes containing Span 80

Run No.	**Formulation Code**	**Vesicular diameter** (µm)	**Entrapment efficiency(%)**
10	B_1	8.24	62.690
11	B_2	8.56	78.705
12	B_3	7.92	81.566
13	B_4	7.80	80.044
14	B_5	8.50	64.863
15	B_6	8.00	75.363
16	B_7	7.25	69.176
17	B_8	8.60	80.111
18	B_9	8.10	60.809

Table: 7 Average Vesicular diameter of Aceclofenac loaded Niosomes containing Span 80.

X_2	**– 1**	0	+ 1
Avg. Vesicular diameter	8.24 (µm)	8.10 (µm)	7.98 (µm)

Table: 8 Average Entrapment efficiency of Aceclofenac loaded Niosomes containing Span 80

X_2	**– 1**	0	+ 1
Avg. Entrapment efficiency	74.32	73.42	70.03

Table: 9 Average Vesicular diameter based on HLB value of Surfactants.

Span	HLB	*x* of batch A/ batch B (µm)
20	8.6	10.63
80	4.3	8.10

***x* = mean average diameter of all x batch A/batch B.**

Table: 10 *In vitro* drug release of Aceclofenac loaded Niosomes containing Span 20

Run No	Time	Average Percentage Drug Release								
		A_1	A_2	A_3	A_4	A_5	A_6	A_7	A_8	A_9
1	00	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
2	01	6.383	4.398	4.237	10.501	25.107	5.237	6.048	5.128	4.687
3	02	10.123	8.498	12.618	20.944	31.059	11.645	15.178	12.412	13.892
4	03	18.503	14.754	16.477	26.678	36.130	15.092	33.615	17.301	23.068
5	04	28.503	21.011	22.901	32.704	42.575	19.054	37.841	26.546	32.373
6	05	42.959	31.809	27.322	39.997	48.527	25.575	47.608	34.702	39.749
7	06	57.158	36.391	32.284	46.186	54.712	31.445	55.380	40.435	46.503
8	07	68.815	44.195	49.281	53.122	62.298	37.270	59.745	48.863	53.552
9	08	78.263	46.671	56.155	61.324	75.250	45.048	66.686	56.474	62.857
10	09	86.974	56.378	59.587	68.422	86.129	50.850	70.967	66.454	74.059
11	10	94.323	59.336	67.090	75.292	95.140	60.917	75.720	76.489	89.708
12	24	99.094	68.764	73.199	82.878	99.796	76.191	84.711	85.734	94.369

Table-11: *In vitro* drug release of Aceclofenac loaded Niosomes containing Span 80

RunNo	Time	Average Percentage Drug Release								
		B_1	B_2	B_3	B_4	B_5	B_6	B_7	B_8	B_9
1	00	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
2	01	8.340	3.903	5.620	5.608	9.196	5.314	7.558	5.433	2.061
3	02	13.818	9.860	12.444	9.063	14.270	15.889	18.098	15.843	8.532
4	03	19.009	15.422	17.661	14.651	21.623	23.496	24.289	22.496	14.521
5	04	23.256	22.517	26.228	19.032	26.433	28.620	30.815	30.327	19.062
6	05	28.939	29.611	29.861	24.414	31.473	35.083	39.347	36.177	26.106
7	06	33.679	34.635	34.648	30.464	36.745	41.132	44.981	41.894	33.542
8	07	40.469	43.962	45.071	36.436	42.248	47.814	51.953	50.661	42.728
9	08	45.127	50.512	49.949	41.151	48.974	55.883	60.894	57.047	48.777
10	09	51.179	58.559	56.343	45.660	55.006	63.587	66.899	66.484	55.519
11	10	58.093	60.452	60.270	56.872	62.260	73.433	74.206	74.342	65.248
12	24	67.754	72.012	64.605	69.831	73.776	89.557	90.135	92.130	86.739

Table-12: Drug release from formulations containing span 20 (Batch A) at $t_{50\%}$

Run No.	**Formulation code**	$t_{50\%}$ (hr. min.)
1	A_1	5.14
2	A_2	7.58
3.	A_3	7.07
4.	A_4	6.34
5.	A_5	5.28

6.	A_6	8.50
7.	A_7	5.24
8.	A_8	7.00
9.	A_9	6.31

Table-13: Drug release from formulations containing span 80 (Batch B) at $t_{50\%}$

Run No.	**Formulation code**	$t_{50\%}$ (hr. min.)
1	B_1	8.47
2	B_2	7.54
3.	B_3	7.58
4.	B_4	8.46
5.	B_5	8.10
6.	B_6	7.09
7.	B_7	6.43
8.	B_8	6.54
9.	B_9	8.06

Table: 14 Kinetic data of Aceclofenac loaded Niosomes Containing Span 20

Batch		Zero Order	First Order	Matrix	Peppas	Hix-Crow
	R	0.8223	-0.9678	0.9112	0.9489	-0.924332
A1	A	4.7051	0.0958	26.8806	1.0492	-0.174484
	B	18.2829	2.1185	-12.0459	0.8394	4.526948
	R	0.8603	-0.9132	0.9405	0.9610	-0.896361
A2	A	3.127	-0.0226	17.6277	0.9858	-0.068858
	B	12.0954	1.9465	-7.5178	0.7251	-4.46857
	R	0.8477	-0.8945	.9258	.9580	-0.879531
A3	A	3.3712	-0.0262	18.9829	0.9718	-0.077526

	B	12.9022	1.9450	-8.1965	0.7675	4.459331
	R	0.8542	0.9266	0.9532	0.9703	-0.904595
A4	A	3.5156	-0.0332	20.2710	0.7072	-0.091482
	B	20.0263	1.9141	-3.0594	1.0980	4.351271
	R	0.8405	-0.9754	0.9467	0.9587	0.95048
A5	A	4.0215	-0.1186	23.3550	0.5202	0.17638
	B	28.251	2.1931	1.4634	1.3597	4.415315
	R	0.9185	-0.9683	0.9576	0.9805	-0.954692
A6	A	3.3852	-0.0276	18.1975	0.9132	-0.078937
	B	9.2408	1.9863	-9.9743	0.7724	4.551621
	R	0.8588	-0.9443	0.9551	0.9613	-0.91852
A7	A	3.7858	-0.0362	21.381	0.8912	-0.09877
	B	18.6776	1.9270	-5.4622	0.9243	4.380819
	R	0.8753	-0.9444	0.9640	0.9428	-0.92460
A8	A	3.9030	-0.0387	-20.1632	0.9758	-0.10230
	B	13.5171	1.9769	-2.1649	0.8132	4.49560
	R	0.9092	-0.9882	-0.9674	0.9515	0.9752
A9	A	3.7200	-0.504	21.8848	0.8216	-0.1161
	B	16.3531	2.0130	-8.1347	0.9126	4.5047

Table: 15 Kinetic data of Aceclofenac loaded Niosomes Containing Span 80.

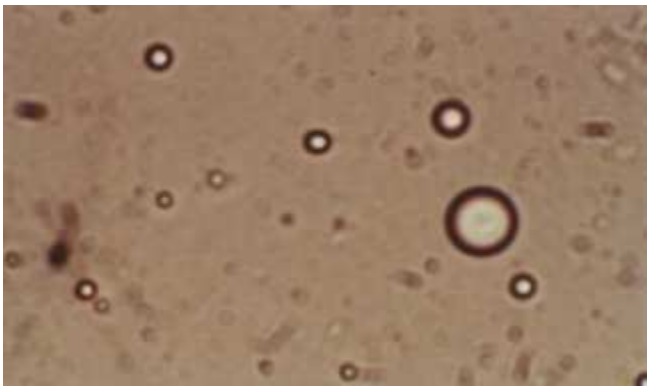
Batch		Zero Order	First Order	Matrix	Peppas	Hix-Crow
	R	0.8850	-0.9343	0.9786	0.9526	-0.9193
B1	A	2.9018	-0.0209	0.7364	0.8131	-0.0640
	B	13.3684	1.9406	-4.6169	0.9705	4.4506
	R	0.8698	-0.9255	0.9434	0.9640	-0.90797
B2	A	3.2760	18.3210	18.3210	1.0048	-0.074
	B	11.8859	1.9532	-8.3299	0.7193	4.480326
	R	0.8329	-0.8724	0.9339	0.9591	-0.8600

B3	A	2.8801	-0.0198	16.6494	0.8509	-0.0623
	B	14.5976	1.9229	-4.4124	0.8602	4.4131
	R	0.9149	-0.9596	0.9595	0.9800	-0.9468
B4	A	3.0922	-0.0229	16.7205	0.8951	-0.0683
	B	9.0745	1.9751	-8.7011	0.7591	4.5370
	R	0.8900	-0.9484	0.9659	0.9798	-0.9312
B5	A	3.3184	-0.0247	17.5616	0.7314	-0.0729
	B	14.5057	1.9418	-4.8841	0.9863	4.4425
	R	0.9033	-0.9824	0.9647	0.9681	-0.9640
B6	A	3.9084	-0.0432	21.5210	0.9100	-0.1084
	B	14.2538	1.9998	-9.0968	0.8851	4.5170
	R	0.8897	-0.9819	0.9653	0.9730	-0.9589
B7	A	3.8843	-0.0439	21.7293	0.8228	-0.1097
	B	16.8597	1.9806	-7.1246	0.9887	4.4652
	R	0.9032	-0.9887	0.9648	0.9694	-0.9708
B8	A	4.0314	-0.0486	22.2036	0.9198	-0.1170
	B	14.5303	2.0181	-9.5673	0.8879	4.5334
	R	0.9273	-0.9883	0.9553	0.9667	-0.9756
B9	A	3.9507	-0.0395	20.9852	1.2174	-0.1023
	B	7.5609	2.0349	-14.2894	0.5254	4.6298

DISCUSSION

Non-ionic surfactants, a cheap, non-toxic biodegradable material has recently gained wide popularity for development of better drug delivery systems. In the present study, non-ionic surfactants, viz., span 20 and span 80 along with cholesterol were used for the development of niosomes for delivery of aceclofenac. Aceclofenac is a non-steroidal anti-inflammatory drug used in osteoarthritis, rheumatoid arthritis and spondylitis.

Aceclofenac loaded niosomes were prepared with the aid of factorial design. Batch (A) containing span 20, cholesterol and aceclofenac in aqueous system were prepared as shown in (table-2) Batch (B) containing span 80, cholesterol loaded with aceclofenac in aqueous system was prepared as shown in (table-2).



Parameters tested include Vesicular diameter and Entrapment efficiency. Vesicular diameter of aceclofenac loaded niosomes containing span 20 presented interesting results. The results indicated that surfactant quantity has an impact on vesicular diameter. Influence of levels of surfactants was examined by altering the concentrations as per factorial design, while keeping amount of cholesterol as constant (100 mg). Vesicular diameter of span 20 formulation A_7 was found to be 10.20µm, the least when compared to other formulations. Average vesicular diameter values for span 20 formulations containing span 20, 100 mg, 120 mg and 140 mg were 10.98(µm), 10.56(µm) and 10.45(µm) respectively(Table-4). Clearly indicating an inverse relationship as amount of span 20 increased there was a decrease in

Vesicular diameter:

Vesicular diameter of aceclofenac loaded niosomes containing span 80 presented similar results. The results indicated that surfactant quantity has an impact on vesicular diameter. Influence of levels of surfactant was examined by altering the concentrations as per factorial design, while keeping amount of cholesterol as constant (100 mg). Vesicular diameter of span 80 formulation B_7 was found to be 7.25(µm), the least when compared to other formulations. Increasing hydrophobicity of the surfactant monomers led to smaller vesicles, a result which is expected since surface free energy decreases with increasing hydrophobicity[7]. Average vesicular diameter values

for span 80 formulations containing span 80, 100 mg, 120 mg and 140 mg were 8.24(µm), 8.1(µm) and7.98(µm) respectively clearly indicating an inverse relationship as the amount of span 80 increased there was a decrease in vesicular diameter(Table7).

The size of the niosomal vesicles prepared is depended on HLB of the span used, the lower the HLB the smaller the initial size of the vesicles, it was observed that span 20 (HLB 8.6) produced niosomes with larger mean vesicle diameter 10.63(µm) in comparison to span 80 (HLB 4.3) with mean vesicular diameter of 8.10(µm).From the microphotographs it is evident that the niosomes were discrete and round in shape.

The encapsulation of different formulations of niosomes containing span 20 listed in table -3 shows that entrapment efficiency in A_2 formulation was the highest 84.44% where as it was 82.62%, 78.66% for formulations A_5 and A_8 respectively, all these formulation contained 120 mg of aceclofenac, whereas in niosomes containing span 80 highest Entrapment efficiency was 81.566% for B_3, whereas lowest Entrapment efficiency was 60.809% for B_9 [Table6].

From the average Entrapment efficiency of Batch A and B formulation containing 100mg, 120mg and 140 mg of aceclofenac it is evident that formulations of span 20 (A) have higher Entrapment efficiency in comparison to span 80 (B) formulations (Table-5&8).

This could be attributed to the structure of surfactants; span 20 has the saturated alkyl chain while span 80 has an unsaturated alkyl chain. The introduction of double bonds made the chains bend. This means the adjacent molecules cannot be tight when they form the membranes of niosomes. This cause the membrane to be more permeable, which possibly explains the lowest Entrapment efficiency of span 80 formulations. It suggests that the alkyl chain is a crucial factor of permeability and saturated chain produces higher entrapment.

The study thus indicates that surfactant quantity has an impact on entrapment. Influence of levels of surfactant examined by altering the total concentration of surfactant keeping the cholesterol factor invariable. Concentration of drug was also varied. Results shows that an increase in the concentration of surfactant decrease the Entrapment efficiency of niosomes (Table-5 & Table-8).

Cholesterol (CH) is one of the common additives included in the formulation in order to prepare stable niosomes. It is also the essential component in niosomes formulation in this study. CH is known to abolish the gel to lipid phase transition of niosomes systems, which could be able to effectively prevent leakage of drug from niosomes[8]. In this study optimum constant quantity of cholesterol is taken for all the formulations. Thus any variation in Entrapment efficiency which could occur due to variable cholesterol is effectively prevented.

In Vitro release of aceclofenac from niosomes were studied using dialysis tube method[9] and drug content determined spectrophotometrically at 275 nm. The release rate of aceclofenac niosomes containing span 20 was highest for A_5 formulation (99.79%), while lowest release (68.76%) was for A_2 formulation (Table10)(Fig 1&2)

From table-12 it is evident that time required for 50% of aceclofenac release from niosomes is in the order $A_6>A_2>A_3>A_8>A_4>A_9>A_5>A_7>A_1$. But total amount of drug release in 10 hour is as follows $A_5>A_1>A_9>A_8>A_7>A_4>A_3>A_6>A_2$ 50% of drug. Thus niosomes showing fastest release are not necessarily highest releasing formulation.

Release rate of aceclofenac niosomes prepared with span 80 is shown in the (figures-4, 5, 6). It is evident that the rate of release is in the order $B_8>B_7>B_6>B_9>B_5>B_2>B_4>B_1>B_3$. B_8shows highest release rate of 74.34% in 10 hours (table-5.3.4.2h) and B_3 shows lowest release of 60.27% in 10 hours (Table-11).

The $t_{50\%}$ values indicate the maximum time required for 50% of release for span 80 formulations in the order of $B_1>B_4>B_5>B_9>B_6>B_3>B_2>B_8>B_7$. (Table-13)

Thus B_1 formulation containing span 80, 100 mg and aceclofenac 100 mg show slowest release 8 hours 47 minutes , while B_7 formulation span 80,140 mg and aceclofenac 120 mg shows fastest release 6 hours, 54 minutes for 50% of drug.

Release mechanism of aceclofenac from niosomal formulations prepared were studied. This data was then treated to study the best linear fit for the following equations[10]:

Percent release = KT … zero order

Log Percent unreleased = Kt / 2.303 … First order

Percent release = $Kt^{0.5}$… Matrix (Higuchi matrix)

Percent unreleased = Kt … Hixson-Crowell.

$$\frac{\text{Amount of drug release at time 't'}}{\text{Amount of drug release at time t}} = Kt^{n}$$ Peppas-Korsmeyer

Percent 'r' is the percentage of drug release at time't', 'k' release rate constant and 'n' is the diffusion coefficient, which is indicative of the transport mechanism and can be used to characterize different release mechanism.

The best fit model for A_5, A_1 and A_9 niosomal formulation was first order type of release. 'r' values equal to 0.9754, 0.9678 and 0.9882 respectively. A_8 showed a release mechanism corresponding to matrix type of diffusion 'r' equal to 0.9640. A_2, A_3, A_4, A_6 & A_7 showed a release corresponding to an anomalous transport, the diffusion coefficient 'n' indicates an anomalous transport release mechanism. The 'n' values between 0.5-1 suggests that more than one type of release phenomenon could be involved (Table-14).

The best fit model for release of aceclofenac from B_6, B_7, B_8 and B_9 was first order mechanism 'r' values 0.9824, 0.9819, 0.9887 and 0.9883 respectively B_1 showed a release mechanism corresponding to matrix type of diffusion 'r' equal to 0.9786. B_5, B_3 and B_4 showed a release mechanism corresponding to anomalous transport 'n' determined by Korsmeyer-Peppas equation was between 0.5-1. B_2 niosomal formulation showed 'n' values of 1.0048, this suggests that case-II transport and super case-II to transport (zero order type release) was observed (Table-15).

***Fig: 1, 2, 3 In vitro* drug release of aceclofenac Loaded niosomes containing Span 20 of Formulation A1, A2, A3, A4,A5,A6, A7,A8,A9**

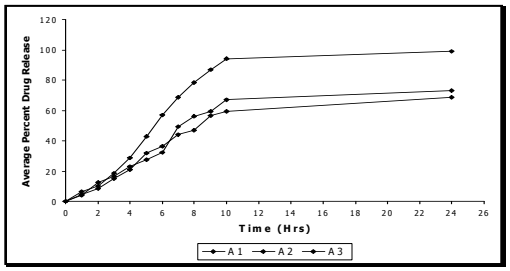


Fig: 1 A1, A2, A3,

Fig: 4, 5.6 In vitro drug release of aceclofenac loaded niosomes containing Span 80 of Formulation B1, B2, B3, B4, B, B6, B7, B8, B9

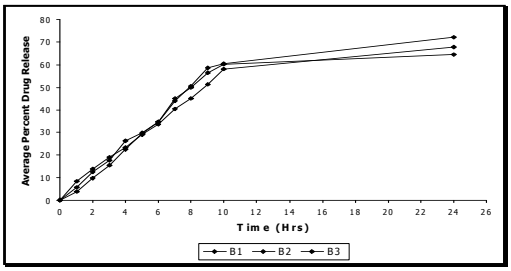


Fig: 4 B1, B2, B3,

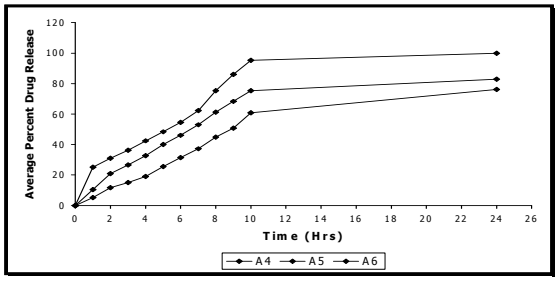


Fig: 2 A4, A5, A6,

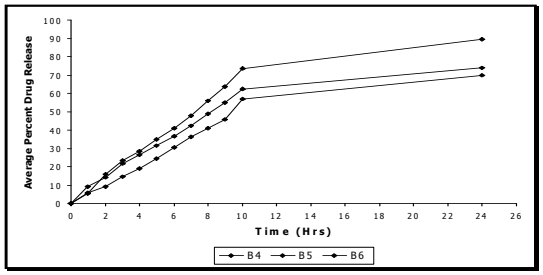


Fig: 5 B4, B5, B6,

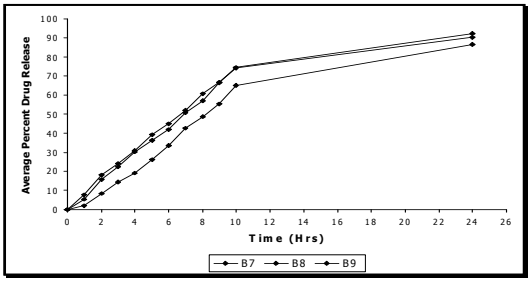


Fig: 3 A7, A8, A9

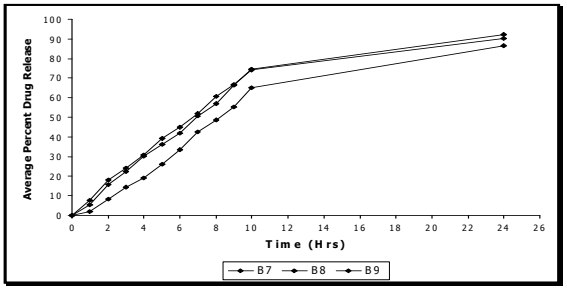


Fig: 6 B7, B8, B9

In the IR spectra of span 20 peak of carbonyl group at 1739 cm^{-1} and a broad peak of 3415 cm^{-1} of OH group is observed. The IR spectra of span 20 formulation (A_5), we observe peak at 1634 cm^{-1} and a broad peak at 2435 cm^{-1} of OH group while there is a disappearance of peaks for NH and NH_2 groups. One may conclude that there is a physical bonding or overlapping of OH group between the constituents of the formulation.

From the IR spectra of span 80 and aceclofenac, we observe carbonyl group peaks at 1742 cm^{-1} and 1716 cm^{-1} and broad peaks of OH groups in span 80 at 3415 cm^{-1}. The IR of cholesterol shows broad peaks of OH group at 3426 cm^{-1}. On observing the formulation-B_8, it is clear that broad peaks of OH at 3434 cm^{-1}, peaks of C=N group is observed at 1637 cm^{-1}, the spectra shows absence of NH and carbonyl group. This suggests that there is a physical interaction between the three compounds.

Fig 7: IR Spectra of Aceclofenac

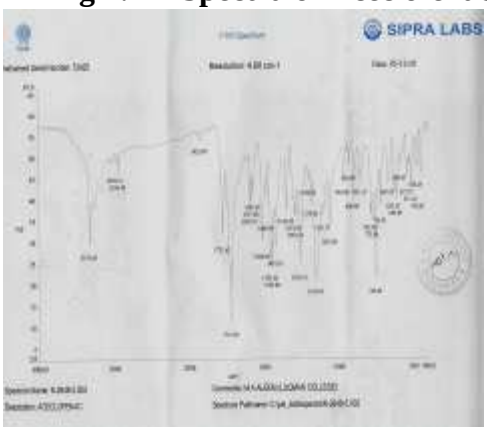


Fig8:IRSpectraofCholesterol

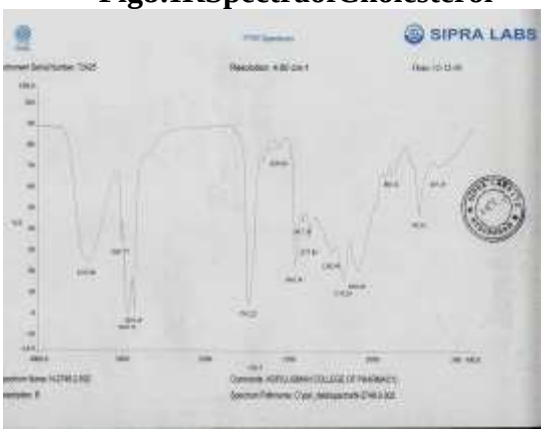


Fig6:IR Spectra of formulation A_5

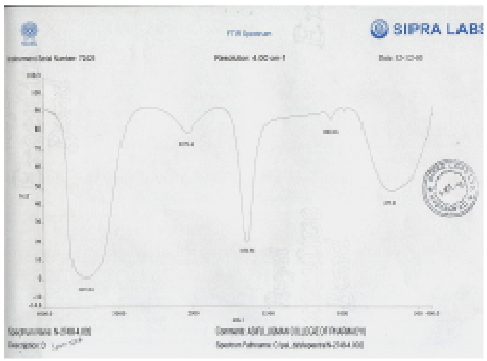
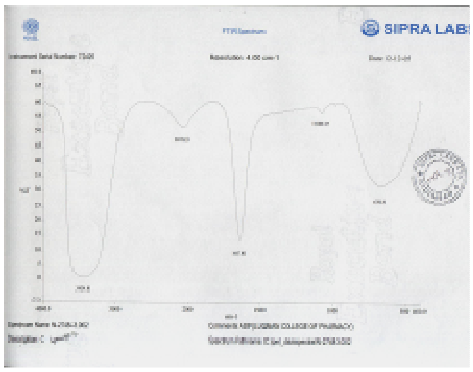


Fig7:IR Spectra of formulation B_8



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Corresponding Author:

Mohamed Hassan Dehghan*

Department of Pharmaceutics,

Y.B. Chauhan College of Pharmacy

Aurangabad, Maharashtra, India.

Email: *mhdehgan@gmail.com*

asifhussainp@yahoo.com