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Research article

FORMULATION AND *IN VITRO* EVALUATION OF NALOXONE TRANSDERMAL PATCHES

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ABSTRACT

While optimizing the topical drug delivery, vesicular system (liposomes and niosomes) appear as upcoming development. Gel system showed topical delivery with higher transdermal flux and higher skin deposition and became an attractive option as it has several desirable advantages. Naloxone is shown to have antifungal activity. It's oral dose is high i.e. 20-200 mg a day and use is limited because of poor intestinal absorption (35%), elimination half life (24 hours) and adverse effects such as Arrhythmia, cardio respiratory arrest, tachycardia, Headache. Hence with the need to modify its route of administration, Gel system containing Naloxone was prepared, characterized and studied for drug release. To confirm the presence of vesicular structure, formulations were visualized under microscope at different magnified fields, which showed presence of lipid bilayer as well as spherical structure of vesicles. Using the same microscopic method and special software "particle size analysis", size of vesicle was determined for sonicated . Vesicular size was found to be in the range of 0 – 5.483 µm. Vesicular size was reduced up to 3 folds by sonication. After confirmation regarding existence of vesicles and their size, drug entrapped by vesicular system was evaluated by ultra centrifugation. Sonicated particles containing 30% w/w ethanol showed higher value i.e. 96.42%. In-vitro release was carried out using dialysis membrane. The values of drug release were F_1 (20% alcohol) 76.89%, F_2 (20% alcohol) 82.31%, F_3 (20% alcohol) 73.62,F_4 (30% alcohol) 96.42%, F_5 (40% alcohol) 72.09%, F_6 (50% alcohol) 72.56%. The order of drug release was found to be first order for all the formulations. Percentage drug accumulation into skin was also found to be maximum by the gel containing 30 % w/w ethanol and 3% lecithin which showed effective subdermal deposition and indicated better subdermal action for hypertension. With these findings it can be summarized that Naloxone gel are promising systems in topical drug delivery for treatment of hypertension.

Key Words:-Transdermal patches, Nalaxone, Emulgel.

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INTRODUCTION

Transdermal therapeutic systems are defined as self-contained discrete dosage forms which, when applied to the intact skin, deliver the drug(s), through the skin, at controlled rate to the systemic circulation (Ravi KJ *et al.*, 2009; Vinupama S *et al*., 2007).

The first Transdermal drug delivery (TDD) system, Transderm-Scop developed in 1980, contained the drug Scopolamine for treatment of motion sickness. The Transdermal device is a membrane-moderated system. The membrane in this system is a microporous polypropylene film (Anamika S *et al.,* 2012). The drug reservoir is a solution of the drug in a mixture of mineral oil and

polyisobutylene (Leon L and Herbert A, 2010; Robinson J and Lee VHL, 1978; Brahmankar DM and Jaiswal SB, 1995). This study release is maintained over a one-day period.

Non-medicated patch markets include thermal and cold patches, nutrient patches, skin care patches (a category that consists of two major sub-categories therapeutic and cosmetic), aroma patches, weight loss patches, and patches thatmeasure sunlight exposure (Chein YW, 1992).

MATERIALS AND METHODS

Materials

Naloxone was gift sample from MSN labs, Hyderabad ltd, India. Propylene glycol, Cholesterol, Carbapol 934,Triethanolamine from Research Lab,Mumbai, India and all other reagents used were of analytical grade and obtained from S.D. Fine chemicals. Mumbai. India.

METHODS

Preparation Of Naloxone (By Cold Method)

Preparation of Naloxone was followed by method suggested by Touitou et al., with little modification[10.]

100mg of Naloxone was dissolved in 6ml of water in a vessel and cholesterol was added to it with vigorous stirring. Propylene glycol was also added during stirring. The contents were heated to 30^0c. In another closed vessel, soy lecithin was dissolved in ethanol with continuous stirring and heated to 30^0 c. When both the solutions reached to same temperature slowly ethanol solution was added drop wise in the centre of vessel containing drug mixture. Then the stirring was continued for another 10min in a covered vessel. Water was added to adjust the volume up to 20 ml (Gennaro RA, 2000; Banker GS and Rhodes CT, 1996).

Cold method for the preparation of Naloxoneemulgel.

Preparation of Naloxone gel

The best achieved vesicle suspension formula EF_4 was incorporated into Carbapol gel (1%, 1.5%, 2% w/w).
The specified amount of Carbapol-934 powder was slowly added to pure water and kept at 100^0c for 20min. Triethanolamine was added to it drop wise. Appropriate amount of formula F_4containing Naloxone was then incorporated into gel-base. Sufficient water was finally added with other formulation ingredients with continuous stirring until homogenous formulation was achieved (G_1, G_2 and G_3). Gel containing free Naloxone drug (100mg) was also prepared by similar method using 1.5% Carbapol (Libo Y, 1999).

CHARACTERIZATION OF ETHOSOMES

Size and shape analysis

Microscopic analysis was performed to determine the average size of prticles. A sample of gel was suitably diluted with distilled water in order to observe individual vesicle and a drop of diluted suspension was put on a glass slide covered with a cover slip. This was examined under microscope (magnification 15 × 45 X). The diameter of 150 vesicles was determined randomly using calibrated eyepiece micrometer with stage micrometer. The average diameter was calculated using the following formula.

$$\mathbf{AverageDiameter}\ (\mathbf{d_{avg}}) = \frac{\mathbf{nd}}{\mathbf{n}}$$

Where

n = number of vesicles
d = diameter of vesicles

Sonication reduced the vesicular size. Since the vesicular size of these vesicles could not be analyzed using microscopic method at magnification 15×45X. Hence analysis of sonicated vesicles was done under a special microscope which was connected with software and photomicrographs were taken under 400 and 800 magnification (Wilson KRW and Waugh A, 1996).

Scanning Electron Microscopy (SEM)

Determination of surface morphology (roundness, smoothness and formation of aggregates) of Naloxone gel with polymer was carried out by using scanning electron microscopy (SEM) (Desai S and Bolton S, 1993).

Entrapment efficiency

The entrapment efficiency of Naloxone dug into vesicle was determined by using ultracentrifugation. 10 ml (Naloxone)of each sample was vortexed for 2 cycles of 5 min with 2 minutes rest between the cycles. 1.5ml of each vortexed sample and fresh untreated Gel formulations were taken into different centrifugal tubes. These samples were centrifuged at 20,000 rpm for 3 hours. The supernatant layer was separated, diluted with water suitably and drug concentration was determined at 234 nm in both vortexed and unvortexed samples.

The entrapment efficiency was calculated as follows

$$\mathbf{EntrapmentEfficiency} = \frac{\mathbf{T - C}}{\mathbf{T}}\ \mathbf{x\ 100}$$

Where
T = Total amount of drug that was detected from supernatant of vortexed formulation
C = Amount of drug unentrapped and detected from supernatant of unvortexed formulation

Characterization Of Gel

Surface morphology

The surface morphology of the gel was determined by scanning electron microscope using gold sputter technique. The system was vacuum dried, coated with gold palladium, and then observed microscopically (Garg S and Sharma S, 2003; Jose and Khalid S, 2003).

Organoleptic Characters

The formulations were tested for their psycho rheological properties like color, odor, texture, phase separation and feel upon application (grittiness, greasiness)

Washability

A small quantity of gel was applied on the skin. After washing with water, it was checked whether the gel was completely washable or not (David SS, 1986).

Spreadability

It was determined by using modified wooden block and glass slide apparatus. A measured amount of gel was placed on fixed glass slide; the movable pan with a glass slide attached to it was placed over the fixed glass slide such that the gel was sandwiched between the two glass slides for 5min. The weight was continuously removed (Sivakumar HG, 2004).

pH measurement

Solution was prepared by dissolving 1gm of Miconazol gel in 30ml of distilled water (pH 7). The pH of gel was determined by using digital pH meter. The measurement was done by bringing the probe of the pH meter in contact with the samples (Singh BN and Kim H, 2003)

Drug content and content uniformity

1g of gel was dissolved in 100mlof phosphate buffer (pH 6.8) and kept for 48 hrs with constant stirring using magnetic stirrer. Then the solution was filtered and the absorbance was observed using U.V spectrophotometer at λmax i.e. 234nm. The measurements were made in triplicate (Choi BY and Park HJ, 2006; Bhavana V *et al*., 1996).

Skin irritation

Rat (male Wristar rat) was taken and the abdominal skin of the rat was clipped free of hair 24 hr prior to the formulation application. 0.5 g of each formulation was applied on the hair-free skin of rat by uniform spreading over an area of 4 cm^2. The skin surface was observed for any visible change such as erythema (redness) after 24, 48 and 72 hr of the formulation application. The mean erythemal scores were recorded depending on the degree of erythema (Ichikawa M *et al.,* 1991).

SKIN PERMEATION STUDIES

Collection Of Semi Permeable Membrane

Semi permeable membrane mimicking skin was prepared by the use of egg membrane. For this an egg was taken and its contents were removed completely by making a small aperture at its tip. Then the egg was dropped in a beaker containing 100ml concentrated Hydrochloric acid (HCl). After about 15min the egg was turned to its other side. Leave the egg in this position for about 30min. The conc. HCl dissolved egg shell leaving behind a semi permeable membrane. This membrane was collected and washed in distilled water thrice so that any remnants of egg or acid will be removed. This gives a semi permeable membrane which can be compared to skin. The membrane was mounted on a modified Franz diffusion cell in such a way that it remained in contact with the donor compartment.

Drug Release Study From Semi Permeable Membrane

The skin permeation of Naloxone from gel formulation was studied using Franz diffusion cell. The effective permeation area of the diffusion cell and receptor cell volume was 2.4 cm and 20 ml respectively. The temperature was maintained at 37 ± 0.5°C [3]. The receptor compartment contained 20 ml of ph 6.8 phosphate buffer which was constantly stirred by magnetic stirrer at 100 rpm. The egg membrane was mounted between the donor and the receptor compartments. 1g of gel formulation was applied to the surface of membrane which was not in contact to the phosphate buffer. The content of diffusion cell was kept under constant stirring. 1 ml of samples were withdrawn from receptor compartment of diffusion cell at predetermined time intervals and analyzed by spectrometric method at 234 nm after suitable dilution. The receptor phase was immediately replenished with equal volume of fresh ph 6.8 buffer. Triplicate experiments were conducted for skin permeation study (Abubakr ON and Jun SZ, 2000).

IN-VITRO RELEASE STUDIES

Drug Release Study From Dialysis Membrane

The skin permeation of Naloxone from gel formulation was studied by using an open ended diffusion cell specially designed laboratory according to the literates. The effective permeation area of the diffusion cell and receptor cell volume was 2.4 cm and 200 ml respectively. The temperature was maintained at 37 ± 0.5°C.

The receptor compartment contained 200 ml of pH 6.8 phosphate buffer and was constantly stirred by magnetic stirrer at 100 rpm. The dialysis was prepared by using semi permeable membrane from egg. The membrane was tied to an open end tube. This served as the donor compartment where as the beaker containing phosphate buffer served as the receptor compartment. Gel formulation [F_1-F_7 (20ml suspension) and for optimized gel (10gm)] was applied to the dialysis membrane and the content of diffusion cell was kept under constant stirring. Then 5 ml of samples were withdrawn from receptor compartment of diffusion cell at predetermined time intervals and analyzed by spectrometric method at 234 nm after suitable dilution. The receptor phase was immediately replenished with equal volume of fresh pH 6.8 buffer. Triplicate experiments were conducted for drug release studies (Sandeep KG *et al.*, 2012; Sameer S *et al.*, 2011).

Stability Studies

Stability study was carried out for Naloxone Gel preparation at two different temperature i.e. refrigeration temperature (4 ± 2° C) and at room temperature (27 ± 2° C) for 8 weeks (as per ICH guidelines). The formulation was subjected to stability study and stored in borosilicate container to avoid any sort of interaction between the Gel

preparation and glass of container, which may affect the observations (Shaji J *et al.*, 1994; Wu W, 1997)

In-vitro stability release study

Stability of drug and stability of vesicles are the major determinant for the stability of formulation. Studies were carried to evaluate total drug content at room temperature (27±2° C) and at refrigeration temperature (4±2° C). Samples were collected for every 2 weeks and absorbance was seen at 234nm in U.V spectrometer.

RESULTS AND DISCUSSION

Preparation of Naloxone (By Cold Method)

Gel formulations composed of phospholipids (lecithin, cholesterol), Naloxone and ethanol were prepared using the method detailed in last chapter titled materials and methods and also according to the literature with little modification in it. gel suspension was slight yellowish in color and hazy in appearance after sonication. Different characteristics of and the effect of sonication were further evaluated and results were reported under characterization.

Characterization

Since the physical characterization is meant for physical integrity of the dosage form, the results were pooled at one place. Discussion on the results, described for gel formulation under the same heading (Blanquet S *et al.*, 2004; Ingani HM *et al*., 1987) .

Size and shape analysis

Microscopic analysis was performed under different magnification to visualize the vesicular structure, lamellarity and to determine the size of gel preparations. The size distribution of Naloxone gel formulations were as shown below

Entrapment Efficiency

Once the presence of bilayer vesicles was confirmed in the gel system, the ability of vesicles for entrapment of drug was investigated by ultra centrifugation. Ultra-centrifugation was the method used to separate the gel vesicles containing drug and un-entrapped or free drug, to find out the entrapment efficiency (Hilton AK and Deasy BP, 1992; Mendhan J *et al.*, 2000; Basak SC *et al.*, 2004).

The maximum entrapment efficiency of gel vesicles as determined by ultracentrifugation was 79.62% for gel formulation containing 30% ethanol (EF4) which was almost double to the formulation containing 50% ethanol (EF6). As the ethanol concentration increased from 20% to 50% w/w, there was an increase in the entrapment efficiency and with further increase in the ethanol concentration (>30% w/w) the vesicle membrane became more permeable and that lead to decrease in the entrapment efficiency. Results of entrapment efficiency also suggest that 3% phospholipid concentration is optimum for entrapment efficiency. Any increase or decrease in concentration of phospholipid reduces the entrapment efficiency of vesicles (Himasankar K *et al.*, 2006; Subrahmanyam CVS, 2001).

Increase in entrapment efficiency may be due to the possible reduction in vesicle size. There is a detrimental effect on the vesicles during ultra-centrifugation which are larger in size. Sonication gives more uniform lamellae with smaller vesicle and uniform size. Hence it may be the reason for higher vesicular stability and lesser vesicular disruption during ultra centrifugation (Chawla G *et al*., 2003; Naim S and Samuel B, 2004; Thomas D and Reza F, 2000).

***In-Vitro* Drug Permeation Studies**

In-vitro skin permeation study or in-vitro diffusion study has been extensively studied, developed and used as an indirect measurement of drug solubility, especially in preliminary assessment of formulation factors and manufacturing methods that are likely to influence bioavailability.

The objectives in the development of in-vitro diffusion tests are to show the release rate and extent of drug from the dosage form. The in-vitro drug permeation study of Naloxone from gel formulation was studied using Franz diffusion cell and the method described in methodology chapter.

The release data was obtained for all the gel formulations. Spectrometric results were obtained and given consideration to sampling loss, to calculate actual cumulative drug diffused was calculated since the volume of receptor cell was only 20 ml (table-24). The obtained diffused amount of drug was extrapolated to diffusion by unit surface area of semi permeable membrane. These cumulative values were plotted as a function of time and steady state transdermal flux was calculated from the slop of linear portion (Figure 27).

Table 1. Composition of different emulgel formulations

Formulation (F)	Lecithin (%)	Propylene Glycol (%)	Ethanol (%)	Cholesterol (mg)	Drug (mg)	Water
F_1	2	10	20	0.05	100	Q.s
F_2	3	10	20	0.05	100	Q.s
F_3	4	10	20	0.05	100	Q.s
F_4	**3**	**10**	**30**	**0.05**	**100**	**Q.s**
F_5	3	10	40	0.05	100	Q.s
F_6	3	10	50	0.05	100	Q.s

F_7	-	10	30	0.05	100	Q.s

* F7- Free suspension without vehicle forming agent.

Table 2. Composition of different gel formulation

Gel formulation	Naloxone Gel suspension(ml)	Carbapol (%)	Tri ethanol amine (ml)	Water
EF_4G_1	20	1	0.5	Q.s
EF_4G_2	**20**	**1.5**	**0.5**	**Q.s**
EF_4G_3	20	2	0.5	Q.s
*G_4	0.025g	1.5	0.5	Q.s

Table 3. Size distribution of gel formulation#1 F_1 (2% Lecithin, 20% ethanol)

Size Range					
Eye piece micrometer	**In µm**	**Average size (d) µm**	**No of vesicles (n)**	**% No of vesicles (n/150 *100)**	**n x d**
0-1	0.00-3.33	1.665	65	43.33	108.225
1-2	3.33-6.66	4.995	62	41.33	309.69
2-3	6.66-9.99	8.325	11	7.33	91.575
3-4	9.99-13.32	11.655	7	4.667	81.585
4-5	13.32-16.65	14.985	5	3.33	74.925
			Σn = 150		**Σnd = 666**

Average diameter (d avg) = $\frac{\Sigma nd}{\Sigma n}$ = 4.44 µm

Table 4. Size distribution of gel formulation#2 F_2 (3% Lecithin, 20% ethanol)

Size Range					
Eye piece micrometer	**In µm**	**Average size (d) µm**	**No of vesicles (n)**	**% No of vesicles (n/150 *100)**	**n x d**
0-1	0.00-3.33	1.665	60	40.000	99.9
1-2	3.33-6.66	4.995	45	30.000	224.775
2-3	6.66-9.99	8.325	30	20.000	249.75
3-4	9.99-13.32	11.655	10	6.667	116.55
4-5	13.32-16.65	14.985	5	3.333	74.925
			Σn = 150		**Σnd = 765.9**

Average diameter (d avg) = $\frac{\Sigma nd}{\Sigma n}$ = 5.106 µm

Table 5. Size distribution of gel formulation#3 F_3 (4% Lecithin, 20% ethanol)

Size Range					
Eye piece micrometer	**In µm**	**Average size (d) µm**	**No of vesicles (n)**	**% No of vesicles (n/150 *100)**	**n x d**
0-1	0.00-3.33	1.665	58	38.667	96.57
1-2	3.33-6.66	4.995	40	26.667	199.8
2-3	6.66-9.99	8.325	27	18.000	224.775
3-4	9.99-13.32	11.655	22	14.667	256.41
4-5	13.32-16.65	14.985	3	2.000	44.955
			Σn = 150		**Σnd = 822.51**

Average diameter (d avg) = $\frac{\Sigma nd}{\Sigma n}$ = 5.483 µm

Table 6. Size distribution of gel formulation#4 F_4 (3% Lecithin, 30% ethanol)

Size Range					
Eye piece micrometer	**In µm**	**Average size (d) µm**	**No of vesicles (n)**	**% No of vesicles (n/150 *100)**	**n x d**
0-1	0.00-3.33	1.665	59	39.333	98.235
1-2	3.33-6.66	4.995	48	32.000	239.76
2-3	6.66-9.99	8.325	26	17.333	216.45

3-4	9.99-13.32	11.655	15	10.000	174.825
4-5	13.32-16.65	14.985	2	1.333	29.97
			Σn = 150		**Σnd = 765.9**

Average diameter (d avg) = $\frac{\Sigma nd}{\Sigma n}$ = 5.062 µm

Table 7. Size distribution of gel formulation#5 F_5 (3% Lecithin, 40% ethanol)

Size Range					
Eye piece micrometer	**In µm**	**Average size (d) µm**	**No of vesicles (n)**	**% No of vesicles (n/150 *100)**	**n x d**
0-1	0.00-3.33	1.665	64	42.667	106.56
1-2	3.33-6.66	4.995	52	34.667	259.74
2-3	6.66-9.99	8.325	23	15.333	191.475
3-4	9.99-13.32	11.655	11	7.333	128.205
4-5	13.32-16.65	14.985	2	1.333	29.97
			Σn = 150		**Σnd = 715.95**

Average diameter (d avg) = $\frac{\Sigma nd}{\Sigma n}$ = 4.71 µm

Table 8. Size distribution of gel formulation#6 F_6 (3% Lecithin, 50% ethanol)

Size Range					
Eye piece micrometer	**In µm**	**Average size (d) µm**	**No of vesicles (n)**	**% No of vesicles (n/150 *100)**	**n x d**
0-1	0.00-3.33	1.665	70	46.667	116.55
1-2	3.33-6.66	4.995	67	44.667	334.665
2-3	6.66-9.99	8.325	7	4.667	58.275
3-4	9.99-13.32	11.655	4	2.667	46.62
4-5	13.32-16.65	14.985	2	1.333	29.97
			Σn = 150		**Σnd = 586.08**

Average diameter (d avg) = $\frac{\Sigma nd}{\Sigma n}$ = 3.907µm

Table 9. Drug entrapment efficiency of Naloxone Gel

Formulation code	Entrapment efficiency (%)			MEAN
F1	72.19	71.75	71.82	71.92
F2	66.91	67.12	68.53	67.52
F3	60.05	60.00	60.01	60.02
F4	**79.91**	**79.62**	**79.33**	**79.62**
F5	58.01	55.96	54.96	56.31
F6	39.39	42.32	42.76	41.49

Table 10. Drug release profile

Time (min)	Cumulative % drug release
0	0
5	3.29
10	6.53
15	10.67
30	17.82
60	19.48
120	22.31
240	28.81
360	32.71
720	46.32
1080	60.21
1440	75.62

***IN-VITRO* RELEASE STUDIES**

Table 11. *In-vitro* cumulative % drug release profile for Naloxone

	Cumulative % drug release						
Time	F_1	F_2	F_3	F_4	F_5	F_6	F_7
0	0	0	0	0	0	0	0
30min	14.56	17.5	12.09	18.09	11.39	10.01	11.21
1hr	25.62	31.52	23.26	32.51	20.21	18.09	13.62
2hr	30.1	38.3	28.21	39.42	25.22	22.31	22.72
3hr	33.08	42.52	32.71	46.42	30.09	27.69	29.32
4hr	38.62	47.81	37.21	49.31	36.21	30.03	30.29
5hr	40.07	54.32	39.05	56.51	37.02	33.61	38.25
6hr	43.62	58.50	43.02	60.41	42.3	37.32	42.91
7hr	66.02	65.41	56.42	76.32	55.21	52.09	49.56
8hr	70.52	73.25	60.31	82.31	61.71	56.31	50.56
9hr	71.61	79.24	68.42	90.43	67.28	60.15	65.34
10hr	76.89	82.31	73.62	96.42	72.09	63.21	72.56

Fig 1. Franz diffusion cell

Fig 2. % Drug release of formulations (F1-F4)

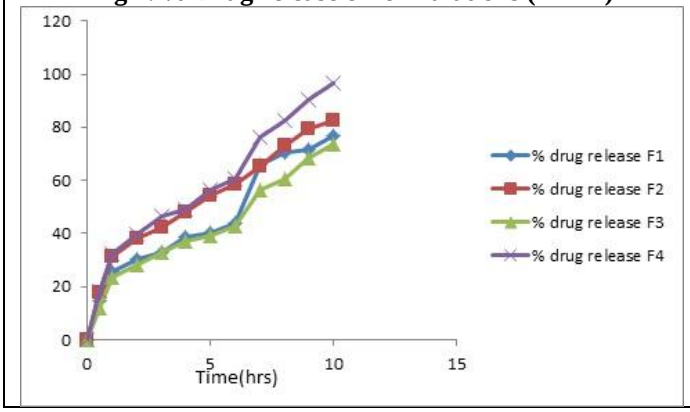
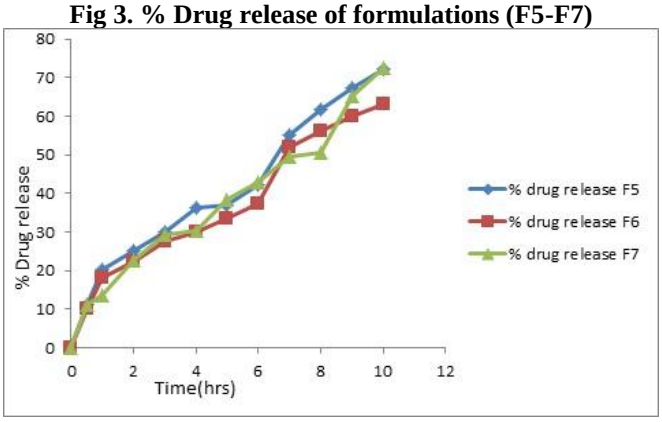


Fig 3. % Drug release of formulations (F5-F7)



SUMMARY AND CONCLUSION

Transdermal route offers several potential advantages over conventional routes. These advantages includes avoidance of first pass metabolism, predictable and extended duration of action, minimizing undesirable side effects, utility of short half-life drugs, improving

physiological and pharmacological response, avoiding the fluctuation in the blood levels, and most important it provides patient convenience. But one of the major problems for efficient drug delivery is low penetration rate.

While optimizing the topical drug delivery, vesicular system (liposomes and niosomes) appear as upcoming development. Gel system showed topical delivery with higher transdermal flux and higher skin deposition and became an attractive option as it has several desirable advantages. Naloxone is shown to have antifungal

activity.It's oral dose is high i.e. 20-200 mg a day and use is limited because of poor intestinal absorption (35%), elimination half life (24 hours) and adverse effects such as Arrhythmia, cardio respiratory arrest, tachycardia, Headache. Hence with the need to modify its route of administration, Gel system containing Naloxone was prepared, characterized and studied for drug release.

To confirm the presence of vesicular structure, formulations were visualized under microscope at different magnified fields, which showed presence of lipid bilayer as well as spherical structure of vesicles. Using the same microscopic method and special software "particle size analysis", size of vesicle was determined for sonicated. Vesicular size was found to be in the range of 0 – 5.483 µm. Vesicular size was reduced up to 3 folds by sonication.

After confirmation regarding existence of vesicles and their size, drug entrapped by vesicular system was evaluated by ultra centrifugation. Sonicated particles containing 30% w/w ethanol showed higher value i.e. 96.42%. In-vitro release was carried out using dialysis membrane. The values of drug release were F_1 (20% alcohol) 76.89%, F_2 (20% alcohol) 82.31%, F_3 (20% alcohol) 73.62,F_4 (30% alcohol) 96.42%, F_5 (40% alcohol) 72.09%, F_6 (50% alcohol) 72.56%. The order of drug release was found to be first order for all the formulations. Percentage drug accumulation into skin was also found to be maximum by the gel containing 30 % w/w ethanol and 3% lecithin which showed effective subdermal deposition and indicated better subdermal action for hypertension. With these findings it can be summarized that Naloxone gel are promising systems in topical drug delivery for treatment of hypertension.

From the present study it can be concluded that Naloxone gel is promising route of drug administration. Even though the TDDS faces the problem of drug permeation because of the rigid stratum corneum, it can be overcome by the use of penetration enhancers such as ethanol. The size of the Gel can be reduced by sonication thereby improving the skin permeation properties of gel. By encapsulating Naloxone gel the frequency of dosing can be reduced as gel cause the delivery of drug for almost 10hrs. Since the overall drug administered is reduced, the adverse drug reactions of Naloxone such as dizziness, allergy, hypotension, etc can also be reduced.

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Nil

CONFLICT OF INTEREST
No interest

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