RESEARCH ARTICLE

DEVELOPMENT AND CHARACTERIZATION OF INVASOMES OF TAZAROTENE FOR POTENT ANTI ACNE EFFECT

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Abstract

Invasomes are novel and flexible vesicles containing a mixture of soy phosphatidylcholine (PC), terpenes, lyso PC, and ethanol with improved skin penetration in comparison with liposomes. Furthermore, invasomes have the same structural constituents as liposomes but contain terpene in their structure. Acne is considered as one of the most widespread skin diseases. When extreme disfiguration occurs, it results in the development of severe consequences among the young people and may result in depression and suicide. Acne vulgaris is the second uppermost reason of suicide among skin diseases. When a person is suffering from acne is compared with an individual who is not suffering from acne than it is found that the former has higher level of anxiety, more socio inhibition and has more aggressiveness. Tazarotene is a compound similar to vitamin A. It helps the skin to renew itself more quickly and may improve the appearance and texture of skin. The brand of tazarotene cream is used to reduce the appearance of fine wrinkles on the face, mottled light and dark skin patches on the face, and benign facial lentigines (non- cancerous freckles) in adults and adolescents who are at least 17 years old.

Key Words- *Invasomes, phosphatidylcholine, terpenes, Acne, Tazarotene, mottled light, benign facial lentigines, adolescents.*

Introduction

Acne is considered as one of the most widespread skin diseases. When extreme disfiguration occurs, it results in the development of severe consequences among the young people and may result in depression and suicide. Acne vulgaris is the second uppermost reason of suicide among skin diseases. When a person is suffering from acne is compared with an individual who is not suffering from acne than it is found that the former has higher level of anxiety, more socio inhibition and has more aggressiveness. Acne is an exclusive disease associated with skin occurs when sebaceous glands (SGs) attain special conditions. This disease occurs in both male and female; there is no preference among them, but the course is more severe in males.

Invasomes are novel and flexible vesicles containing a mixture of soy phosphatidylcholine (PC), terpenes, lyso PC, and ethanol with improved skin penetration in comparison with liposomes.

Furthermore, invasomes have the same structural constituents as liposomes but contain terpene in their structure. Terpenes are hydrocarbon compounds and are known to be the primary constituents of essential oils from many plants. Addition of terpenes creates deformable vesicles, which can increase the fluidity of the lipid bilayers of the skin.
Tazarotene is a compound similar to vitamin A. It helps the skin to renew itself more quickly and may improve the appearance and texture of skin. The brand of tazarotene cream is used to reduce the appearance of fine wrinkles on the face, mottled light and dark skin patches on the face, and benign facial lentigines (non- cancerous freckles) in adults and adolescents who are at least 17 years old. The Fabior and Tazorac brands of tazarotene topical are used to treat acne vulgaris in adults and adolescents who are at least 12 years old. Tazorac is also used to treat plaque psoriasis (raised, silvery flaking of the skin) in adults.

Material and Ingredients

Tazarotene was obtained from Bioplus Life Sciences Pvt. Ltd.Bangalore, Phosphatidylcholines was obtained from Thomas Baker, Mumbai, Disodium Hydrogen Phosphate, Di potassium Hydrogen Orthophosphate, Carbopol 934p, Methyl Paraben, Propyl Paraben, Propylene Glycol and Sodium Chloride was obtained from S. D. Fine Chem. Ltd., Mumbai. Methanol, Ethanol, Chloroform was obtained from S. D. Fine Chem. Ltd., Mumbai

Preformulation Studies

Preliminary stability studies involve chemical, physiochemical and, when necessary, microbiological tests. Stability studies are sometimes thought of as concerning only chemical stability but the stability of physiochemical characteristics are also important. These are some examples of preformulation studies are- Organoleptic properties, particle shape, size, Melting point, solubility, partition coefficient etc.

Method of Preparation

Tazarotene was loaded in to invasomes by mechanical dispersion technique. Soya Phosphatidylcholine (0.5 to 1% w/v) was added to ethanol and vortexed for 5 minutes [75-76]. Drug and terpenes (0.5 to 1.5%) were added under constant vortexing, this mixture was sonicated for 5 minutes. Fine stream of Phosphate buffer saline (upto 10% w/v) was added with syringe under constant vortexing. It was vortexed for additional 5 minutes to obtain final invasomal preparation.

Table 1: Formulation optimization of Tazaroteneloaded Invasomes

Ingredient (%)	F1	F2	F3	F4	F5	F6
Tazarotene (mg)	50	50	50	50	50	50
Phosphotidylcholine (%)	0.5	0.5	0.5	1	1	1
Terpenes (%)	0.25	0.25	0.25	0.5	0.5	0.5
Ethanol (ml)	5	5	5	5	5	5

Table 2: List of Sensory characters

S. No.	Sensory characters	Result
1.	Taste	Tasteless
2.	Appearance	Light yellow powder
3.	Odor	Odorless

Solvent used	Results of Solubility
Distilled Water	Insoluble
0.1 N Hydrochloric acid	Soluble
0.1 N NaOH	Soluble
Ethanol	Freely soluble
Methanol	Freely soluble
Chloroform	Soluble
Phosphate buffer pH 7.4	Soluble

Table 3: Solubility of Tazarotene

S. No.	Melting Point of Tazarotene	Average Melting Point of Tazarotene
1.	95-96°C	95-96°C
2.	94-95°C	
3.	95-96°C	

Table 4: Melting point of the Tazarotene

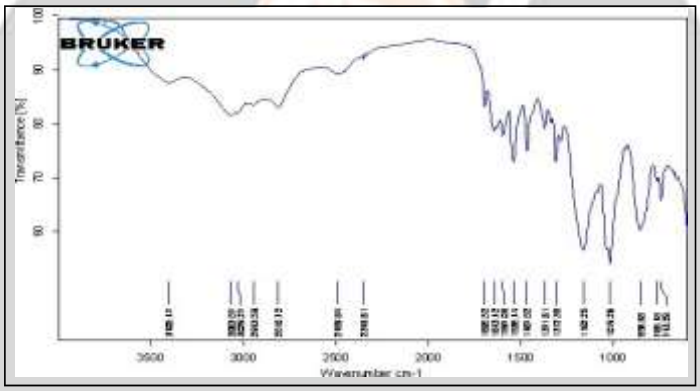


Fig. 1: FT-IR Spectrum of Pure Drug (Tazarotene)

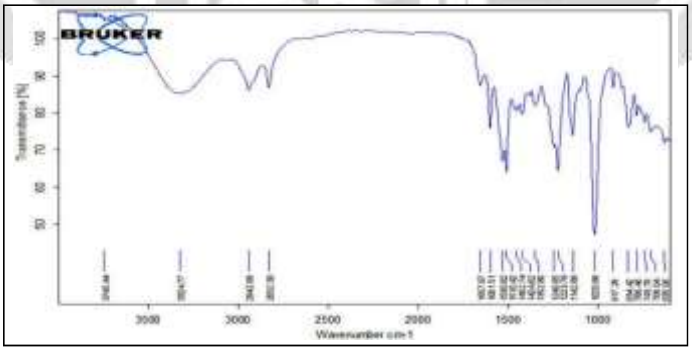


Fig. 2: FT-IR Spectrum of Pure Drug and Excipients

S. No.	Drug	KF Factor	Amount of KF Reagent consumed	Moisture content
1	Tazarotene	0.547	0.2ml	0.1094

Table 5: Moisture content determination

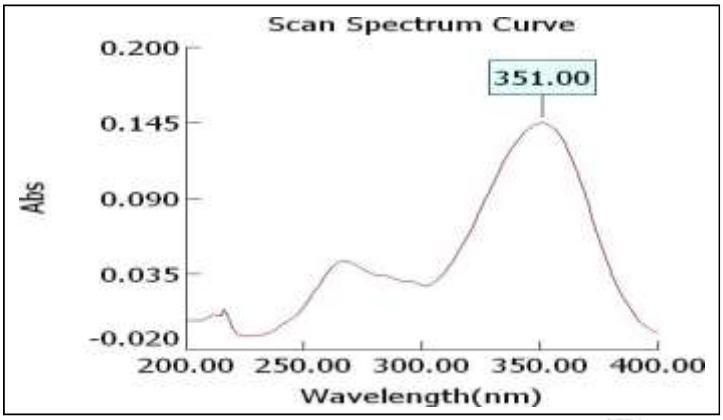
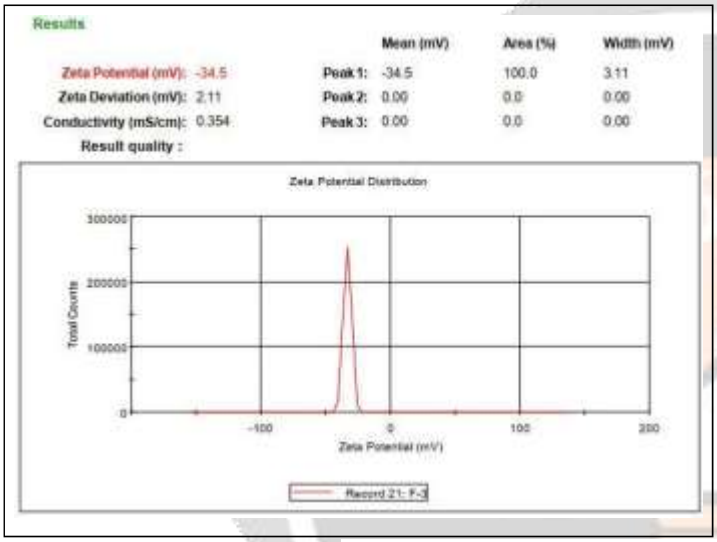


Fig. 3- Wavelength maxima of tazarotene in phosphate buffer pH 7.2



S. No.	Concentration (µg/ml)	Absorbance
1	10	0.218
2	20	0.402
3	30	0.594
4	40	0.826
5	50	1.054

Table 6: Calibration curve of Tazarotene

Formulation Code	% Entrapment efficiency	Average vesicle size (nm)
F1	65.58 ± 0.25	256.65 ± 0.25
F2	68.54 ± 0.36	312.56 ± 0.32
F3	63.32 ± 0.14	285.45 ± 0.45
F4	65.56 ± 0.35	345.58 ± 0.41
F5	76.65 ± 0.24	220.14 ± 0.25
F6	69.95 ± 0.18	256.65 ± 0.54

Table 7: Entrapment efficiency and average vesicle size

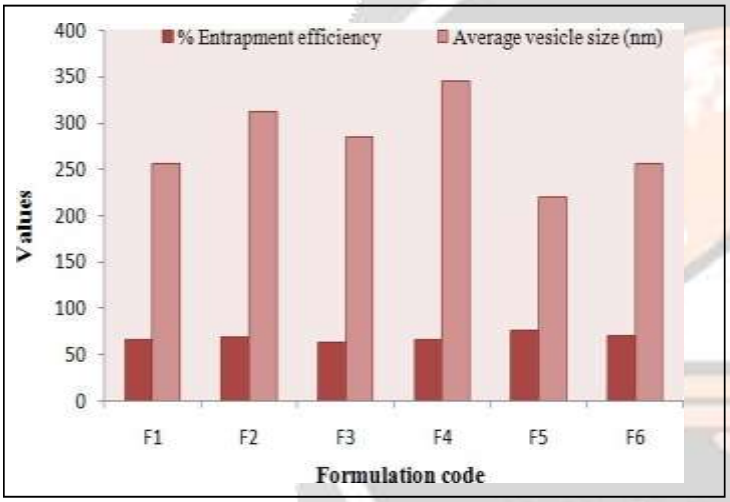


Figure 4: Graph of % entrapment efficiency and average vesicle size of all formulation F1 to F6

Figure 5: Graph of zeta Potential (mV) optimized formulation F-5

Gel formulation	Viscosity (cps)	pH	Drug Content (%)	Extrudability (g)	Spreadibility (g.cm/sec)
IG-1	3565±15	6.75±0.02	96.65±0.15	145.5±0.5	11.25±0.25
IG-2	3325±12	6.82±0.03	99.12±0.25	165.6±0.4	10.23±0.32
IG-3	3045±14	6.98±0.02	98.58±0.32	163.1±0.2	9.85±0.14

Table 8: Characterization of gel based formulation of Invasomes

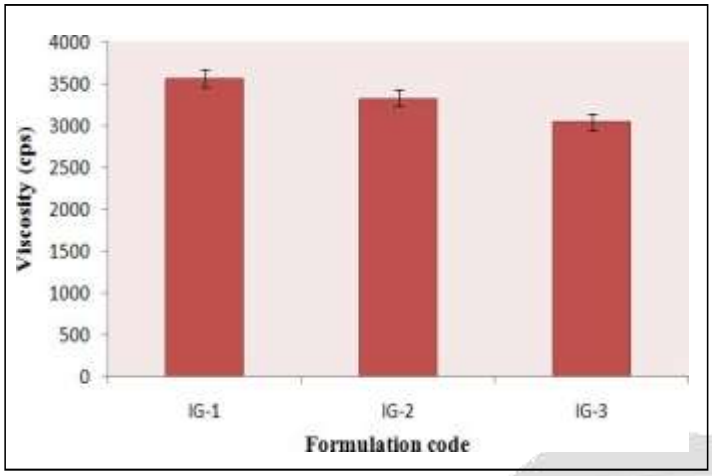


Figure 6: Result of viscosity (cps) of formulation IG1 to IG3

S. No.	Time (hr)	% Cumulative Drug Release*
1	0.5	11.25±0.25
2	1	23.36±0.32
3	2	36.65±0.45
4	4	43.32±0.65
5	6	64.74±0.21
6	8	79.98±0.14
7	10	89.95±0.25
8	12	98.85±0.33

Table 9: *In vitro* drug release study of prepared optimized gel formulationIG-2

Table 10: Release kinetics of Invasomes encapsulated formulation IG-2

Time (h)	Square Root of Time(h)$^{1/2}$	Log Time	Cumulative*% Drug Release	Log Cumulative % Drug Release	Cumulative % Drug Remaining	Log Cumulative % Drug Remaining
0.5	0.707	-0.301	11.25	1.051	88.75	1.948
1	1	0	23.36	1.368	76.64	1.884
2	1.414	0.301	36.65	1.564	63.35	1.802
4	2	0.602	43.32	1.637	56.68	1.753
6	2.449	0.778	64.74	1.811	35.26	1.547
8	2.828	0.903	79.98	1.903	20.02	1.301
10	3.162	1	89.95	1.954	10.05	1.002
12	3.464	1.079	98.85	1.995	1.15	0.061

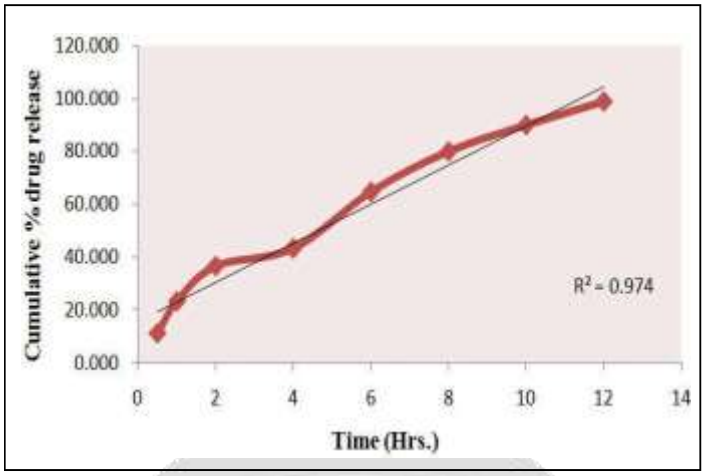


Figure 7: Cumulative % drug released Vs Time (Zero Order Kinetics)

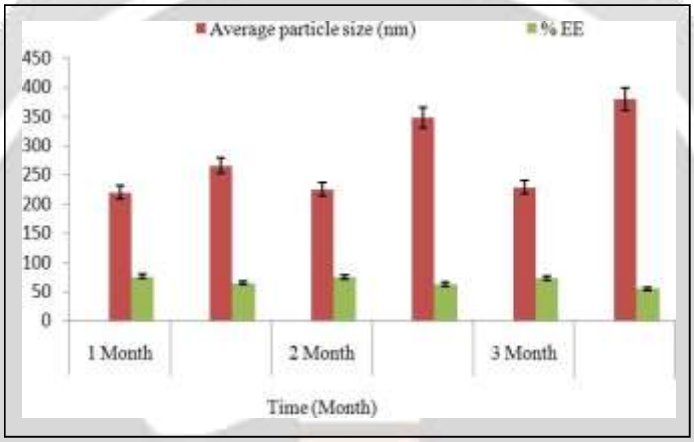


Figure 8: Graph of stability study of optimized formulation of Invasomes

Summary and Conclusion

In present study was to develop and characterize tazarotene -loaded invasomal drug carrier systems. Different Formulations (F1 to F6) of invasomes were prepared and evaluated for average vesicle size, zeta potential and entrapment efficiency.

The Average vesicle size was found to be in the range of 220.14 ± 0.25 to 345.58 ± 0.41, the minimum vesicle size was found in formulation F-5, 220.14 ± 0.25 nm.

The Entrapment Efficiency of formulations F1. F2, F3, F4, F5 and F6 was found to be 65.58 ± 0.25, 68.54 ± 0.36, 63.32 ± 0.14, 65.56 ± 0.35, 76.65 ± 0.24 and 69.95 ± 0.18 percentage respectively.

The maximum percentage entrapment efficiency was found to be in formulation F-5, 76.65 ± 0.24 percentages.

The pH of theGel was found to be in range of 6.75 ± 0.02 to 6.98 ± 0.02 which is good for skin pH. All the formulation of Gel was shown pH nearer to skin required i.e. pH of IG1- 6.75 ± 0.02, IG2-6.82 ± 0.03 and IG3-6.98 ± 0.02.

Drug content of tazarotene incorporated invasomes gel for formulation IG-1, IG-2 and IG-3 was found to be 96.65 ± 0.15**,** 99.12 ± 0.25 and 98.58 ± 0.32 respectively. The maximum drug content was found in formulation IG-2 (99.12 ± 0.25), select as optimized formulation.

When the regression coefficient values of were compared, it was observed that ‘r’ values of korsmeyer peppas was maximum i.e. 0.979 hence indicating drug release from formulations was found to follow korsmeyer peppas kinetics. In conclusion, the invasomes delivery systems may be a promising carrier for transdermal delivery of tazarotene for the management of treatment of acne.

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