10. Stability Study

10.1. Introduction

Stability of pharmaceutical product is critical to product quality and needs to be thoroughly investigated to recommend an appropriate storage condition and to establish the shelf-life. These studies commonly involve evaluation of any change in products' critical quality attributes with respect to time when exposed to different environmental conditions such as of temperature, relative humidity and light. Stability study of all developed formulations were performed as per ICH guidelines-Q1A(R2) of stability testing of new drug substances and products.(1)

10.2. Materials and Methods

10.2.1. Materials

Cubosomes of TAC, TAC cubosomes microneedle patch, cubosomes FBX and FBX cubosomes microneedle patch were developed and characterized in-house. Sorbipak (Silica gel sachets) was purchased from Sorbead India. Calcium oxide was purchased from LobaChemie Pvt. Ltd., India. Double distilled water was prepared in lab, filtered through 0.2µ membrane filter in glass bottle and consumed within a maximum of 7 days.

10.2.2. Short term stability study of cubosomes and cubosomes loaded MNP

Short term stability of all developed formulation as described above were studied at 30±2 °C/65±5 %RH for three months. AFF, in-vitro dissolution time of MNP and entrapment efficiency, vesicle size and PDI of cubosomes were considered as critical attributes and therefore selected as stability indicating characteristics of cubosomes and cubosomes loaded MNP. Patches were hermetically packed in airtight high density plastic containers along with silica gel and calcium oxide as desiccant. Cubosomal dispersions were stored in air tight container. These containers were stored in stability chamber operating at 30±2 °C/65±5 %RH for three months. Samples were withdrawn every month and evaluated for critical stability indicating parameters using the methods described earlier in this chapter.

10.3. Results and Discussion

10.3.1. Short term stability study

The AFF and in vitro dissolution time of MNP and vesicle, PDI and percent drug entrapped of cubosomes stored for up to three months are summarized in **Table 10.1**.

Table 10.1: Three month stability data of cubosomes and cubosomes loaded MNP

Formulation	Time (months)	AFF (N)	In vitro dissolution time (min)	Vesicle size (nm)	PDI	% Entrapment
TAC cubosomes loaded gel	Initial	-	-	158.4 ± 6.84	0.184 ± 0.021	93.15 ± 3.68
	1 M	-	-	167.3 ± 7.25	0.190 ± 0.018	92.24 ± 3.15
	2 M	-	-	172.0 ± 6.81	0.191 ± 0.023	91.95 ± 4.13
	3 M	-	-	176.7 ± 5.73	0.195 ± 0.015	91.61 ± 2.94
TAC cubosomes loaded MNP	Initial	1.10 ± 0.05	1.5	155.8 ± 7.45	0.179 ± 0.018	95.74 ± 6.47
	1 M	1.08 ± 0.06	1.5	157.1 ± 5.17	0.194 ± 0.02	95.04 ± 4.84
	2 M	1.03	1.5	157.9 ±	0.197	94.58 ± 5.14

		± 0.08		6.87	± 0.034	
	3 M	0.95 ± 0.04	1.5	158.6 ± 3.84	0.211 ± 0.024	95.07 ± 3.48
FBX cubosomes loaded gel	Initial	-	-	156.1 ± 6.81	0.214 ± 0.031	88.79 ± 4.15
	1 M	-	-	160.4 ± 4.87	0.197 ± 0.015	88.54 ± 3.29
	2 M	-	-	158.49 ± 7.8	0.215 ± 0.021	89.58 ± 5.81
	3 M	-	-	162.3 ± 5.54	0.238 ± 0.035	87.29 ± 3.14
FBX cubosomes loaded MNP	Initial	0.90 ± 0.04	1.25	153.9 ± 6.25	0.213 ± 0.015	87.04 ± 2.84
	1 M	0.88 ± 0.03	1.25	155.7 ± 4.94	0.210 ± 0.014	87.96 ± 3.95
	2 M	0.83 ± 0.05	1.25	158.2 ± 6.18	0.204 ± 0.020	88.57 ± 4.65
	3 M	0.81 ± 0.04	1.25	162.8 ± 5.68	0.201 ± 0.017	89.25 ± 3.14

Values represented as mean ± SD

On storage, AFF was slightly decreased in all four formulations while there is no effect on in vitro dissolution time of developed MNP. Similarly, a slight increase in vesicle size and PDI as well as a slight decrease in drug entrapment was evident on storage in both cubosomal formulations. However, the values observed after three months were found within desirable limits required for formulations to perform effectively. Such observation at intermediate temperature and high relative humidity could interpret that solid MN patch should be stored in air tight container with silica bag to absorb moisture content while cubosomal dispersion should be stored in air tight container at room temperature.

10.4. References

1. Guideline IHT. Stability testing of new drug substances and products. Q1A (R2), current step. 2003;4:1-24.