CHAPTER VI

CLINICAL STUDIES

6.1 INTRODUCTION

A clinical trial is a method for comparing objectively, by a prospective study, the results of two or more therapeutic procedures. Before clinical trials came into being, methods of treatment were chosen on the basis of clinical impressions and personal experience rather than objective testing. Although many drugs, with undoubted effectiveness remain in use without ever having been subjected to a controlled clinical trial, any new drug or new dosage form of an existing drug is now required to have been tested in this way before being licensed for general clinical use.

Based on the results of the <u>in vivo</u> blanching studies, it was deemed worthwhile to compare the efficacy of one liposomal formulation each of TRMA(T_7), FLU(F_2) and CLO (C_2) with their respective free drug gels in patients with dry bilateral eczema and psoriasis. A study was also conducted using the liposomal (C_2) and free (KCG) gels of CLO in a solitary candidate with keloids.

6.2 EXPERIMENTAL

6.21 Preparation of samples :

Free and liposomal gels of TRMA (0.01% w/w), FLU (0.025 % w/w) and CLO (0.05% w/w) were prepared and filled into lacquer coated aluminium tubes. The open end of the tube was crimped securely. Each tube contained 20 g of the

preparation. The tubes of the free and liposomal gels of each drug were coded by alphabet A and B, not respectively, by a person not involved in the study.

6.22 Trial methodology

A double blind clinical trial was conducted for the drugs under study in patients with dry bilateral eczema and psoriasis. The trials for TRMA gels were conducted by the physician incharge Skin VD and leprosy section, Department of Medicine, Govt. Medical College, Aurangabad while those for FLU and CLO by the Head, Skin VD, Sri Sayaji General Hospital, Baroda. Patients with bacterial infection or any other systemic illness eg. Diabetes mellitus were excluded from the study. Each patient was given Tube A and Tube B of one drug with the instructions to apply the contents on two different sites which were clinically identical, twice daily, after cleaning the local part with luke warm water. Patients were instructed, not to use any medication, systemic or topical, during the one month trial period. The progress was assessed on weekly basis by the physician and the findings duly filled in the datasheet of the patient. The grading of the change in the lesions was left to the discretion of the physician in charge. A representative datasheet designed for this study is shown in Fig.6.1.

6.23 Keloid Case

History : The patient had keloids on the back and chest since the age of 12 years. The recommended treatment was cosmetic

FIG 6.1

A REPRESENTATIVE DATASHEET FOR THE DOUBLE BLIND CLINICAL TRIAL OF (TRMA/FLU/CLO) GELS.

PATIENT'S NAME :
AGE :
SEX :
OCCUPATION :

ECZEMA/PSORIASIS

PROVISIONAL DIAGNOSIS :
AREAS INVOLVED :

DETAILS OF TREATMENT ADMINISTERED PREVIOUSLY

SYSTEMIC :
LOCAL :
DURATION :

DETAILS OF PRESENT TREATMENT

DATE OF STARTING TREATMENT :
DRUGS CO ADMINISTERED :
RESPONSE :

TIME	TUBE A	TUBE B
1st week		
2nd week		
3rd week		
4th week		

DOCTOR'S COMMENTS ON THE PATIENT'S PROGRESS WITH RESPECT TO TUBE A & TUBE B :-

Trial conducted by :- Dr.
Name of institution :-

Address of institution :-

Gels supplied by :- PHARMACY DEPARTMENT
FACULTY OF TECH. & ENGG.
M. S. UNIVERSITY OF BARODA
BARODA - 390 001.

surgery or injecting TRMA into the fibrous mass. Since both the treatments were considered to be too drastic, the keloids had been left untreated.

Trial details : After consultation with the Head, Skin VD department, Sri Sayaji General Hospital, Baroda, it was considered worthwhile to try the free and liposomal gels of CLO on these keloids, as a test case. Hence 2 keloids (Plate 6.1) which were almost similar in size, dark brown in color and hard were selected for the study. The patient was to apply the coded gels, once daily on the overgrowth for a period of 15 days followed by a 15 days off period till satisfactory changes were seen. At the end of 30 days, the dimensions of the keloids were measured along predecided axis, using a vernier callipers.

6.3 RESULTS AND DISCUSSIONS

(a) TRMA gels : The trial was conducted on 9 patients with eczematous dermatitis and 3 patients with psoriasis. The responses were graded in terms of good, better and excellant with respect to the original condition. 4 patients with eczematous dermatitis showed excellent response at free TRMA gel site while three at the liposomal TRMA gel site. Two patients were lost in follow up. 2 patients with psoriasis showed better response at the T_7 site while one at the KTG site. No statistically significant differences were found to exist in the efficacy of free and liposomal TRMA gels.

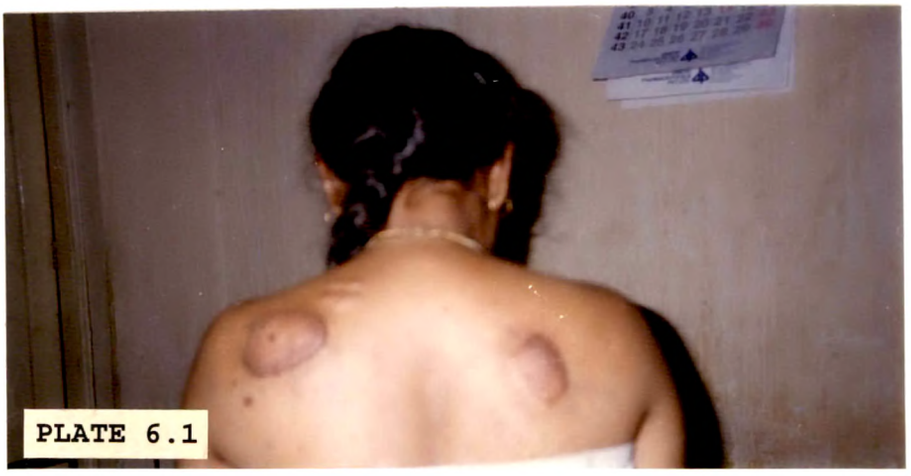


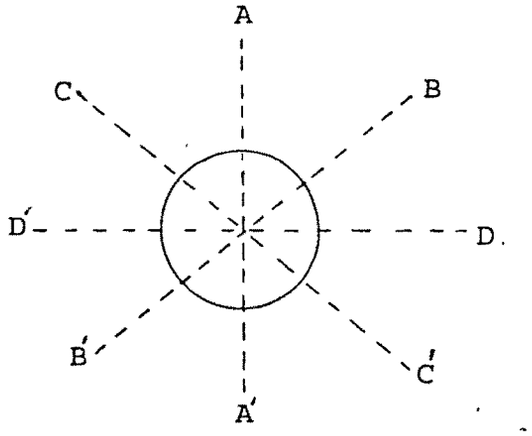
PLATE 6.1

(b) FLU gels : The trial was conducted on 10 patients with dry bilateral eczema. The responses were graded in terms of percentage improvement with respect to the original condition. 2 patients were lost in follow up. At the end of one month, the percentage improvement ranged between 20-70%. The mean percentage improvement in the eczematous condition was higher for the free FLU gel (36.75%) as compared to that for the liposomal FLU gel (30.25%). However, when the comparison was made using the student's t-test, the calculated t-value (1.134) exceeded the Table-t value only at $P<0.4$ indicating that no significant differences exist between the efficacy of the two formulations in patients with eczema.

(c) CLO gels : The trial was conducted on 10 patients with dry bilateral eczema. Weekly responses were graded in terms of percentage improvement with respect to the original condition. 3 patients were lost in follow up. At the end of the month, the percentage improvement ranged between 30-80%. The mean percentage improvement in the eczematous condition was higher for the liposomal CLO gel (45-96%) as compared to the free CLO gel (39.23%). However, when the comparison was made using the student's t-test, the calculated t-value (1.525) exceeded the Table-t value only at $P<0.4$ indicating that no significant differences exist between the efficacy of the two formulations in patients with eczema.

TABLE 6.1

CHANGES IN THE DIMENSIONS OF KELOIDS FOLLOWING TREATMENT WITH FREE CLO GEL (KCG) AND LIPOSOMAL CLO GEL (C_2).



Axis of measurement

AXIS	DIMENSIONS (CMS) OF KELOID TREATED WITH KCG				DIMENSIONS (CMS) OF KELOID TREATED WITH C_2			
	INITIAL	1 mth	2 mths	3 mths	INITIAL	1 mth	2 mths	3 mths
AA'	4.69	4.60	4.59	4.31	4.89	4.65	4.52	4.23
BB'	6.22	5.99	5.95	5.25	4.41	3.30	3.09	3.00
CC'	5.96	5.40	5.31	4.84	3.92	3.05	3.04	2.88
DD'	5.94	5.90	5.79	5.68	3.75	2.89	2.86	2.82

The least count of the vernier callipers used was 0.01 cms.

(d) Keloïd Case : The changes in the dimensions of the keloids over a 3 month period are shown in Table 6.1. The average percentage reduction in size of the keloid treated with KCG was 11.71% while that of the keloid treated with C_2 was 24.20% over a 3 month period. Since the gels were used on two different keloids, no direct comparisons can be made. Keloids have also reduced in thickness - a factor not monitored in the study. They have become lighter in color and soft. The study is under progress.

Due to the lack of availability of a large number of patients, the results of the clinical trials cannot be considered conclusive. However it can be noted that there is no compromise in the efficacy when liposomal topical corticosteroids are used in patients with eczema.