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In vivo evaluation of framycetin cream and ketoconazole ointments for the treatment of melanoma cancer in animal models

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Abstract
A variety of factors can lead to melanoma cancer, including ultraviolet light, carcinogenic substances, and genetic factors. Group 2 was exposed to DMPA-TPA-induced skin cancer, which was compared with group 1 (normal control group). In histopathology studies, group 3, which was treated with an anticancer drug, showed a reduction in skin colour and shape. In the
framycetin-treated group, cancer was significantly reduced compared to the ketoconazole-treated group. The differences in normal SGOT and SGPT levels are likely due to inflammation affecting different groups. The differences in normal SGOT and SGPT levels are likely due to inflammation affecting different groups.
Keywords*: Cancer, melanoma, DMPA, TPA, skin*

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I. INTRODUCTION

Melanoma cancer is related to the skin and affects dermatitis. Melanoma is a neoplasm that arises from melanocytes in the mucosa [1]. it accounts for more than 80% of skin cancer. The incidence of melanoma has increased worldwide. This could be observed in Australia and other countries like New Zealand and Denmark [2].

The melanoma genome has the highest mutation burden of any cancer and a predominant nucleotide transition related to UV radiation [3], [4].

Framycetin is used for the treatment of bacterial blepharitis, conjunctivitis, and corneal injuries [5]. It works by binding to specific 30S-subunit proteins and 16S rRNA [6], this region interacts with the wobble base in the anticodon of tRNA, which leads to interference with the initiation complex, and misreading of mRNA. Ketoconazole is an imidazole antifungal, used in the prevention and treatment of a variety of fungal infections [7]. Ketoconazole works by interacting with 12-a-sterol demethylase,a cytochrome-P-450 enzyme that is important for the conversion of lanosterol to ergosterol, this results in the inhibition of ergosterol synthesis and increased fungal cellular permeability [8].

II. MATERIALS & METHODS

the drugs framycetin and ketoconazole were brought from Uniq Health Care. Carcinogenic TPA and DMPA were brought from Unitron Bio-Medicals. Animals from Aditya Bios-Bangalore (approval No IAEC-NCP09/2023/02 Nargund College of Pharmacy -Bangalore 560078.

Dermal toxicity has already been studied for ketoconazole and framycetin. The albino mice weighing 22 to 28 g were shaved at uber dorsal 10% and kept for three days. DMPA single dose of 2μl/ animal was given for groups 2,3,4 and 5. After one-week TPA 5 μl was given to groups 2,3,4 and 5 for eight weeks after papilloma started appearing [9], and tobramycin and ketoconazole were given for ten days.

On the 10^{th} week, blood was withdrawn by retroorbital method for SGOT, SGPT and CRP. animals sacrificed by a high dose of anaesthesia. Tissues of samples were taken for histopathology studies from each group of studies [10].

Table 1, Animal Groups

S.No	Animals Grouping	1st week	2nd to 8th weeks	9th to 10th Weeks
Group 1	Normal Control	NA	NA	NA
Group 2	Tumor-bearing mice	DMPA 2μl	TPA 5 μl	NA
Group 3	Tumor-bearing mice + stander Drug Fu-5	DMPA 2μl	TPA 5 μl	Fu-5
Group 4	Tumor-bearing mice + framycetin	DMPA 2μl	TPA 5 μl	1% framycetin
Group 5	Tumor bearing mice + ketoconazole	DMPA 2μl	TPA 5 μl	10% ketoconazole
Group 6	Tumor-bearing mice + framycetin and ketoconazole	DMPA 2μl	TPA 5 μl	1% framycetin +10% ketoconazole

III. RESULTS

Table 2, Blood parameters

S NO	SGOT U/L	SGPT U/L	CRP MG/DL
GROUP 1	32.0±3	33.0±3	<4
GROUP 2	66.5±9	70.5±9	<5
GROUP 3	41.6±1	45.6±1	<3
GROUP 4	29.0±3**	30.0±3**	<4
GROUP 5	30.0±3**	29.0±3**	<3
GROUP 6	50.0±3**	56.0±1***	<4

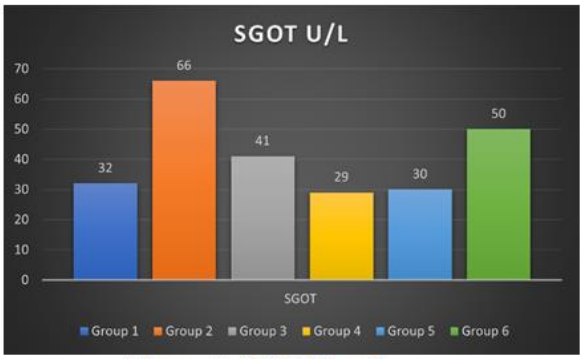


Figure 1, SGOT Level

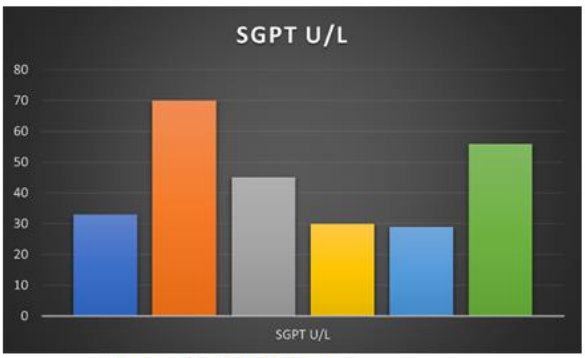
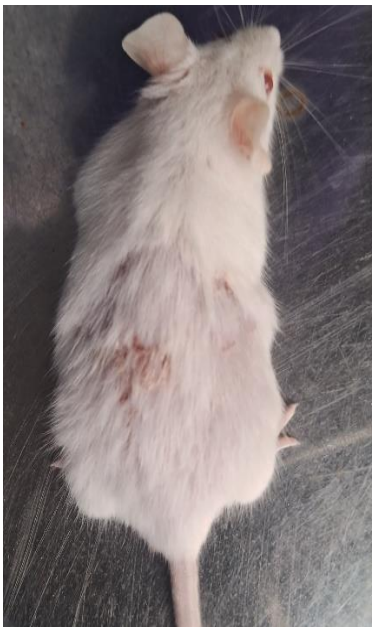
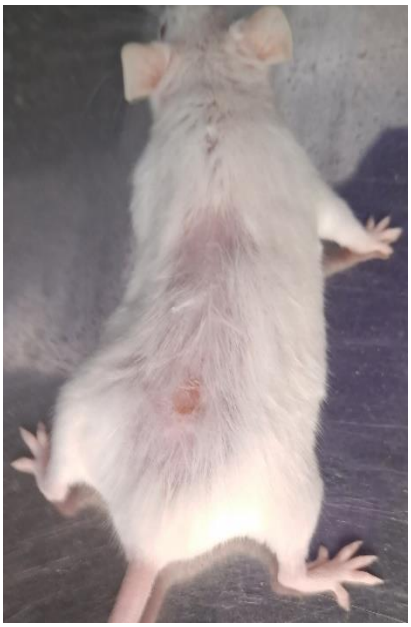
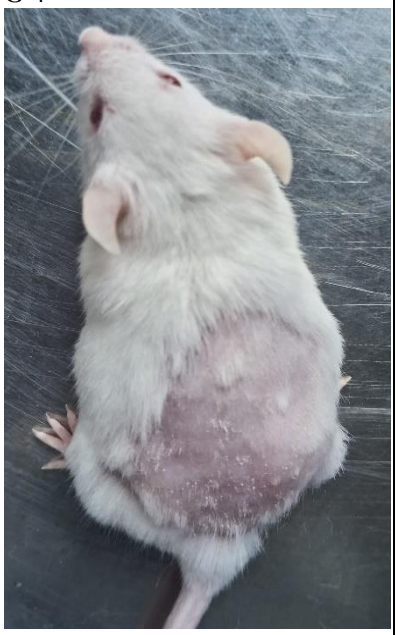
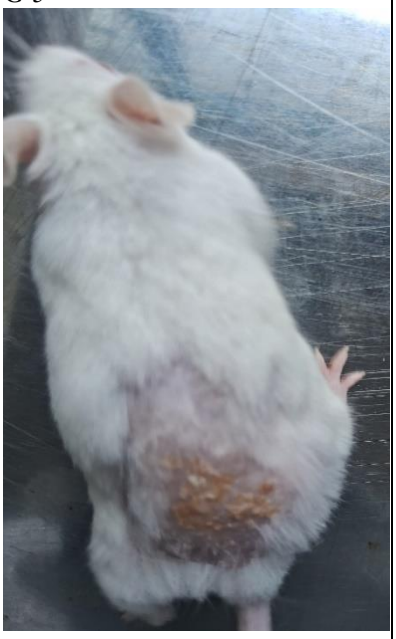
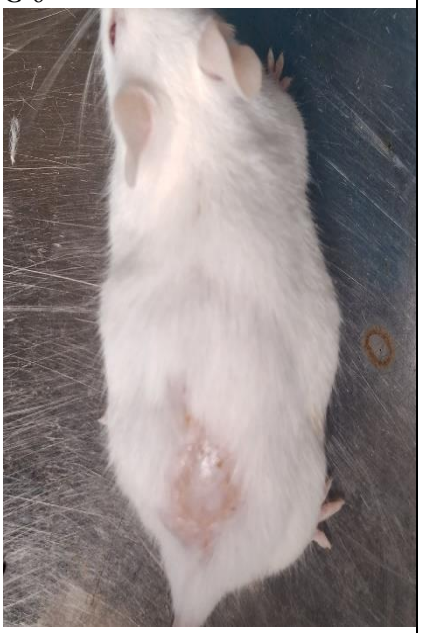


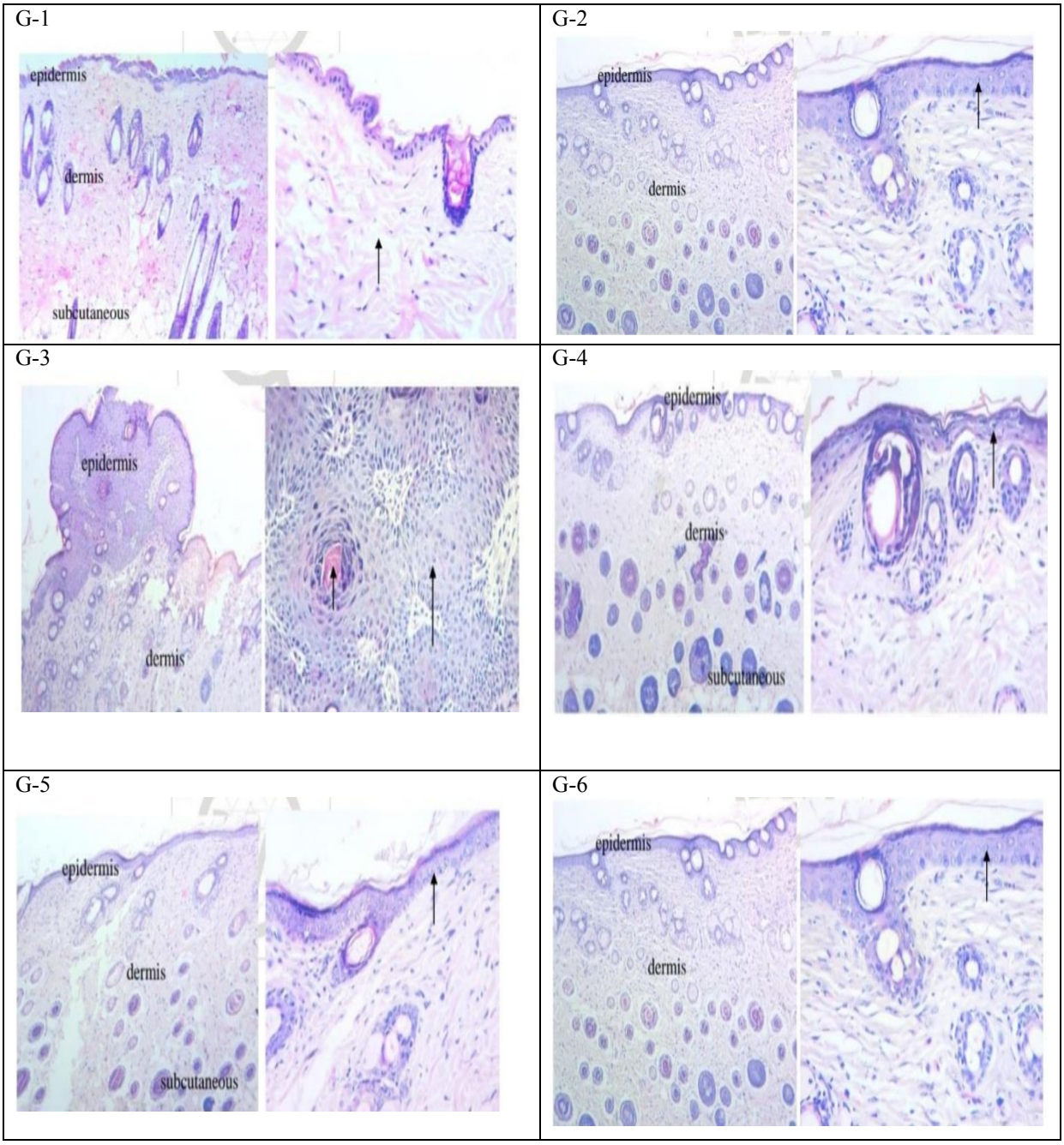
Figure 2, SGPT Level

IN VIVO STUDIES

In the normal control group, the skin appeared normal compared to the 2nd group, with no significant melanoma cells. The 3rd group showed moderate changes in the skin. This may be due to the DMPA-TPA dose, which initially caused a change in dermal shape which led to the growth of tumor cells. Due to Fu-5's anticancer properties, group 4 showed less change. As a result, sofraymcin and ketoconazole significantly altered the levels in groups 5 and 6. Sofraymcin showed that although there is no significant difference in the long-term regarding drug combinations, after topical application, it produced a neutrophilic infiltration, due to the PK-C activation stimulating proinflammatory cytokine production.

G-1 	G-2 	G-3 
G-4 	G-5 	G-6 

HISTOPATHOLOGY STUDIES



Figure, G1 mice show a normal skin area. Still, no clear cells indicate that there is no inflammation in the dermal mice skin, compared to the disease group "DMBA-TPA treatment group. Figure, G2 "disease group show tumor cells present compared to the normal control group and treatment group epidermis -irregular thickness of epidermis (tumor) with proliferation of dysplastic keratinocytes having vesicular nucleus and prominent nucleoli indicated by long arrow in the figure, G2. In Figure-G3, Fu-5 showed a good response in the mice affected with cancer, uniform thickness consisting of stratum corneum, granular layer, spinous layer, and basal layer. Few dysplastic cells are noted in" arrow 2". In group 4 uniform thickness of the epidermis consisting of stratum, fibroblasts with collagen bundles, mid-chronic inflammation, intact blood vessels, hair follicles and sebaceous glands, subcutaneous tissues appear intact, treatment with soframycin and ketoconazole showed moderate effect in mice with DMBA-TPA treated group squamous carcinomas in each group. Data represented mean ±SD. *P<0.05, **P<0.01.*

IV. DISCUSSION

Nearly 85% of all skin cancers are caused by UV radiation, the most important cause. UV exposure triggers acute inflammation in the skin by stimulating the production of proinflammatory cytokines and it is homolog D-DT. Framycetin act as a strong antibiotic and has a different mechanism of action on bacteria rRNA 16s and 30S subunit. Ketoconazole also has an effective role in combination with Framycetin

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CONFLICTS OF INTEREST: Nil

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