HISTOLOGICAL LESIONS IN HPV16-TRANSGENIC MODEL: THE EFFECT OF HIDROETHANOLIC EXTRACT OF *LAVANDULA PEDUNCULATA* (MILL.) CAV.

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INTRODUCTION

The K14HPV16 mice is a skin squamous carcinoma model that can be used to test antitumoral properties of several chemical and natural compounds[1]. The K14HPV16 mice model expresses all the early HPV16 genes under of the cytokeratin 14 (Ck14, *Krt14*) gene promoter and develop cervical and cutaneous lesions[2].

Lavandula penduculata (Mill.) Cav., known as lavender, belongs to the Laminaceae family and has been used in traditional medicine as infusions to treat several conditions. A recent study was shown to have anti-inflammatory and antiproliferative properties[3].

AIM

This work aimed to evaluate the effects of the hydroethanolic French lavender extract (FLE) in an HPV16-transgenic mice model lesions.

METHODOLOGY

Study design and animal procedures were approved by the University of Trás-os-Montes and Alto Douro Ethics Committee (10/2013) and the Direção Geral de Alimentação e Veterinária (0421/000/000/2014). The extract was obtained through a maceration with ethanol/water (80:20, *v/v*) and its phenolic composition was determined by HPLC-DAD-ESI/MS. The FLE was dissolved in drinking water at 6.8 mg/10mL/animal and the animals were supplemented during 29 consecutive days.

Twenty-eight male mice were randomly divided into four groups: (n=7/group): group I (HPV16-control); II (HPV16- FLE); III (HPV16+ control) and IV (HPV16+ FLE). After 29 days all animals were sacrificed by xylazine-ketamine overdose following cardiac puncture to obtain blood samples. Skin samples (chest and ear), kidney, liver and spleen were processed for histological analysis.

RESULTS

A total of thirteen compounds were identified in the hydroethanolic extract, being salvianolic acid B and rosmarinic acid the main molecules present. Moreover, the compounds revealed to be stable in the drinking water for 5 days.

Table 1. Number of animals (%) with histological skin, liver and kidney lesions.

Groups Skin chest lesions	Normal	Epidermal hyperplasia	Epidermal dysplasia
I (HPV16-control)	6/6 (100.0%)	0/6 (0.0%)	0/6 (0.0%)
II (HPV16- FLE)	7/7 (100.0%)	0/7 (0.0%)	0/7 (0.0%)
III (HPV16+ control)	0/4 (0.0%)	4/4 (100.0%)	0/4 (0.0%)
IV (HPV16+ FLE)	0/6 (0.0%)	4/6 (66.67%)	2/6 (33.33%)
Groups Skin Ear lesions	Normal	Epidermal hyperplasia	Epidermal dysplasia
I (HPV16-control)	5/5 (100.0%)	0/5 (0.0%)	0/5 (0.0%)
II (HPV16- FLE)	6/6 (100.0%)	0/6 (0.0%)	0/6 (0.0%)
III (HPV16+ control)	0/5 (0.0%)	3/5 (60.0%)	2/5 (40.0%)
IV (HPV16+ FLE)	0/6 (0.0%)	2/6 (33.33%)	4/6 (66.67%)
Groups Kidney lesions	Normal	Interstitial nephritis	
I (HPV16-control)	4/7 (57.14%)	3/7 (42.86%)	
II (HPV16- FLE)	6/7 (85.71%)	1/7 (14.29%)	
III (HPV16+ control)	3/5 (60.0%)	2/5 (40.0%)	
IV (HPV16+ FLE)	4/7 (57.14%)	3/7 (42.86%)	
Groups Liver lesions	Normal	Hepatitis grade I	Hepatitis grade II
I (HPV16-control)	4/7 (57.14%)	0/7 (0.0%)	3/7 (42.86%)
II (HPV16- FLE)	7/7 (100.0%)	0/7 (0.0%)	0/7 (0.0%)
III (HPV)	4/5 (80.0%)	0/5 (0.0%)	1/5 (20.0%)
IV (HPV16+ FLE)	7/7 (100.0%)	0/7 (0.0%)	0/7 (0.0%)
Groups Spleen lesions	Normal	White pulp hyperplasia	
I (HPV16-control)	6/7 (85.71%)	1/7 (14.29%)	
II (HPV16- FLE)	6/7 (85.71%)	1/7 (14.29%)	
III (HPV16+ control)	5/5 (100.0%)	0/5 (0.0%)	
IV (HPV16+ FLE)	4/7 (57.14%)	3/7 (42.86%)	

Histological analyses of skin samples from wild-type mice exposed (group II) and not exposed (group I) to FLE showed normal skin histology. Group III showed skin chest epidermal hyperplasia in 100% of the mice while group IV showed less epidermal hyperplasia frequency (66.6%) ($p>0.05$). Concerning to liver, kidney, and spleen lesions there in no differences between groups ($p>0.05$).

CONCLUSION

The lavender extract did not prevent the progression of HPV-16 induced cutaneous lesions in this model. These data deserve more investigation to clarify the effect of lavender extract on HPV-16 lesions.

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