HEMATOLOGICAL ASPECTS OF *PTERIDIUM* SPP. (BRACKEN FERN) TOXICITY IN K14-HPV16 TRANSGENIC MICE

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INTRODUCTION

Pteridium spp. (PTE), also known as bracken fern, is a plant species that adapts well to different environmental conditions and is found all over the world [1]. It is a toxic plant that can cause various diseases in animals, such as intestinal and bladder tumors and hemorrhagic diathesis [2]. Cattle may present with leukopenia and thrombocytopenia after prolonged consumption [2].

PURPOSE OF THE EXPERIMENTAL

The objective of this work was to evaluate hematological parameters (hematocrit, hemoglobin, erythrocytes, leukocytes, lymphocytes, platelets) in *wild-type* (WT) mice and mice genetically modified for HPV16 exposed to freeze-dried PTE fiddleheads.

METHODS

This study was approved by UTAD's ORBEA and DGAV (014139). We used 30 female mice, aged between 23 and 25 weeks, in our study. A diet containing freeze-dried PTE fiddleheads of three concentration was administered as a food: 12.5% PTE, 25% PTE, and 50% PTE. Mice were divided into six groups (G1 to G6, n=5): G1 (WT, control), G2 (WT, 50% PTE), G3 (HPV, control), G4 (HPV, 12.5% PTE), G5 (HPV, 25% PTE), and G6 (HPV, 50% PTE). Throughout the 28-day study, we recorded the mice's body mass, food intake, and water consumption. Animals' welfare was monitored during the experiment. At the end of the study, we euthanized the animals and collected blood and samples.

G1 (WT, control) | **G2 (WT, 50% PTE)** | **G3 (HPV16, control)** | **G4 (HPV16, 12.5% PTE)** | **G5 (HPV16, 25% PTE)** | **G6 (HPV16, 50% PTE)**

RESULTS

In general, water and food consumption was higher in transgenic animals from G3, G4, G5 and G6 (Figure 1).

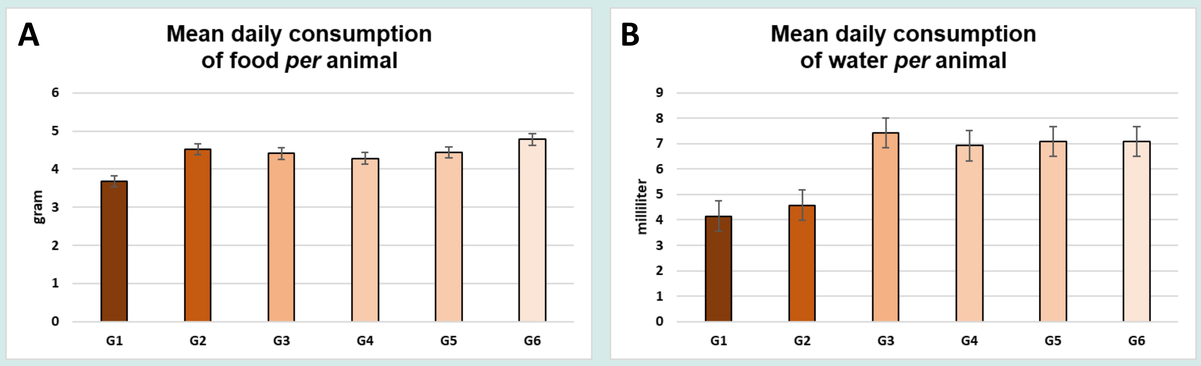

Figure 1. (A) mean daily consumption of food *per* animal; **(B)** mean daily consumption of water *per* animal.

Regarding weight gain, there were no statistically significant differences ($p<0.05$), however, we observed greater gains in WT mice (Figure 2).

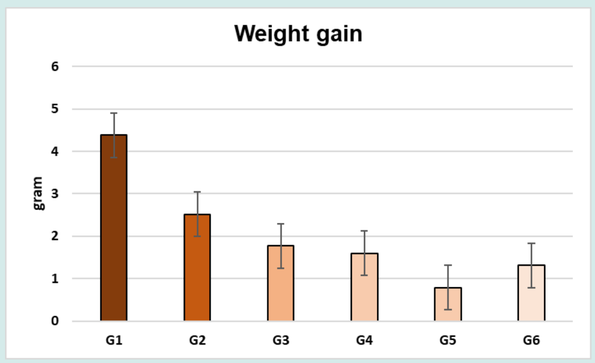

Figure 2. Weight gain *per* group.

The humane endpoints (HE) score was higher in groups 3, 4, 5 and 6, but no animal reached the critical score (4) that would require sacrifice before the experimental testing.

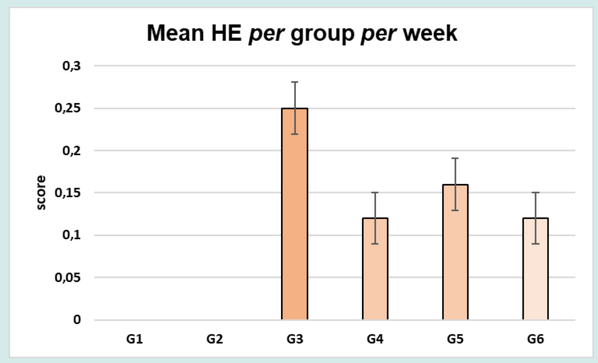

Figure 3. Mean HE *per* group *per* week.

Hematocrit (HCT) was higher in G1 and G6. Hemoglobin (HGB) was higher in the groups that consumed the extract. Erythrocytes (ERI) and glucose were lower in the groups that consumed the extract. G6 showed higher values of leukocytes (LEUK), lymphocytes (LYM), and platelets (PLQ) compared to controls.

Table 1. Hematological parameters evaluated (mean ± standard deviation).

Parameters	G1 (WT, control)	G2 (WT, 50% PTE)	G3 (HPV, control)	G4 (HPV, 12.5% PTE)	G5 (HPV, 25% PTE)	G6 (HPV, 50%)
HCT	48.10 ± 2.24	47.96 ± 1.61	46.30 ± 1.39	46.18 ± 2.62	45.16 ± 2.03	47.28 ± 1.40
HGB	15.06 ± 0.55	15.28 ± 0.61	14.44 ± 0.50	14.74 ± 0.67	14.56 ± 0.55	15.00 ± 0.42
ERI	9.71 ± 0.58	9.60 ± 0.17	9.77 ± 0.13	9.64 ± 0.43	9.57 ± 0.33	9.62 ± 0.37
LEUK	3.15 ± 0.88	3.43 ± 0.95	3.56 ± 1.21	3.19 ± 0.85	3.23 ± 0.50	4.76 ± 1.36
LYM	2.26 ± 0.41	2.29 ± 0.60	2.28 ± 0.68	1.84 ± 0.73	1.83 ± 0.36	2.90 ± 1.03
PLQ	637.80 ± 279.58	535.20 ± 167.96	875.40 ± 389.96	947.60 ± 399.20	983.20 ± 163.18	823.80 ± 139.64
Glucose	159.60 ± 32.49	144.60 ± 21.42	179.60 ± 38.23	150.00 ± 41.44	135.60 ± 30.42	156.60 ± 41.75

HCT: Hematocrit (%); HGB - hemoglobin (g/dL); ERI: erythrocytes (M/ul); LEUK: leukocytes (K/uL);PLQ: platelets (K/uL).

CONCLUSION

In conclusion, the increase in these parameters may reflect the presence of HPV16 transgenes that are enhanced by the extract. However, further studies are underway to better understand the relationship between the extract and HPV16.

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