

## MACRO AND MICROSCOPE ASPECTS IN THE 5-FU-INDUCED ORAL MUCOSITIS MODEL

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In the experimental model of Oral Mucositis (MO), it is possible to observe both the macroscopic and the microscopic aspects that are characteristic of the ulcerative phase, which are similar to that described in the oncology clinic, and which interfere in the quality of life and compliance of patients under chemotherapy [1-2].

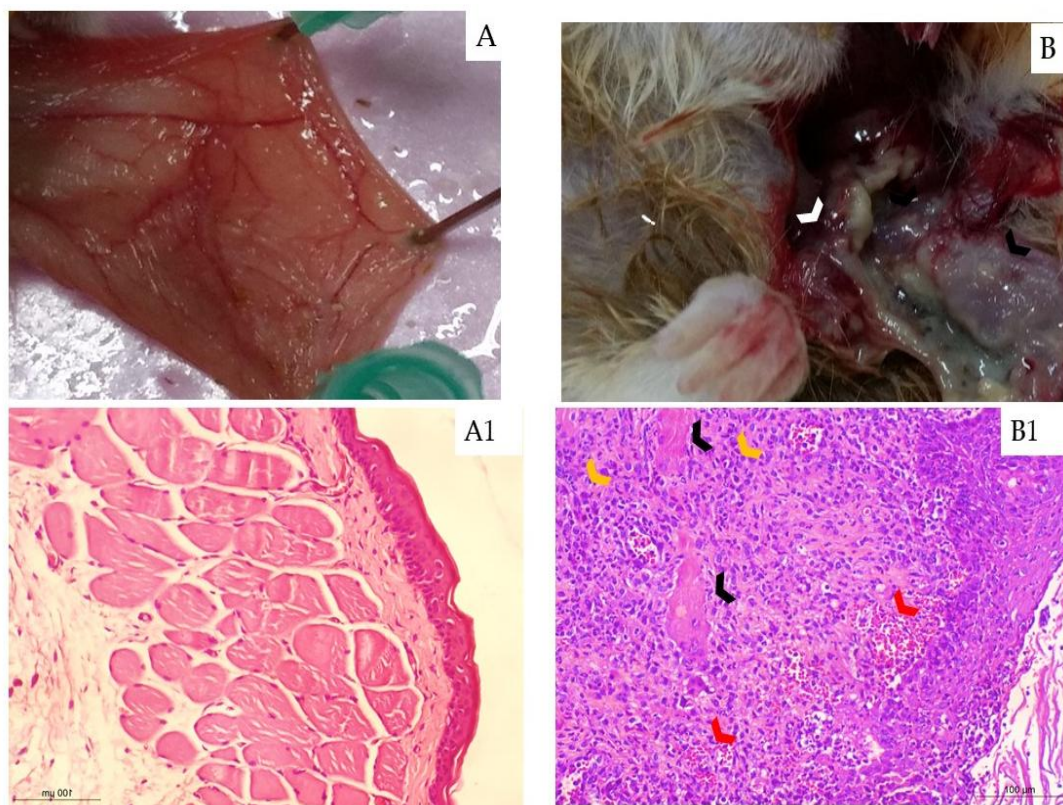
The OM model established in the present study, based on and adapted from the study by Leitão et al. [3], was characterized by the administration of doses of 60 and 40 mg / kg, intraperitoneally, of 5-FU on the 1st, 2nd day, respectively. In addition, on the 4th day, excoriations were made, using a blunt-tipped needle, on the cheek mucosa of the animals that were administered 5-FU doses, observing the development of the inflammatory condition for 10 days.

Figures 1A shows the macroscopic aspects of the oral mucosa of hamsters that were not submitted to 5-FU. In the image it can be identified that the cheek mucosa is preserved, receiving a macroscopic score of 0, that is, without evident clinical changes.

When evaluating figure 1B, we see the group of animals exposed to the induction of MO by the administration of 5-FU. In these animals it was possible to verify areas of ulcers on one or more faces of the jugal mucosa, affecting more than 50% of the surface of the pouch, being difficult to expose, with areas of abscess, severe erythema and hemorrhage (Figure 1B, shown in black arrows and white, respectively). Such findings are characteristic of the macroscopic score of 5, representing a greater number of evident clinical changes.

In the histological analysis, by means of Hematoxylin and Eosin staining, it was observed that in the group of animals that were not exposed to 5-FU, tissue integrity and absence of phlogistic signs were observed, receiving a microscopic score of 0 (Figure 1A1 ). On the other hand, in the group of animals exposed to 5-FU, it was possible to identify a marked

inflammatory infiltrate, high vascular engorgement (hemorrhage) and the presence of abscesses and ulcers, which resulted in the loss of integrity of the jugal epithelium (Figure B1 arrows: black, orange, red, respectively). For these microscopic characteristics, a score of 5 was assigned.



**Figure 1.** Macro and microscopic aspects of the 5-FU-induced oral mucositis model. In panel A and A1 (normal group), normal mucosa is covered by stratified non-keratinized squamous epithelium that is found under the connective tissue lâmina, which is in continuity with the skeletal muscle tissue. In panel B and B1 (group 5-FU) note formation of ulcers, abscesses (black arrow), marked infiltration of inflammatory cells (orange arrow) and vascular engorgement (red arrow and white arrow) (panel B1).

Our findings reaffirm that the chemotherapy 5-FU triggers, with clinical fidelity, the picture of oral

mucositis in experimental models, being observed through the categorization of the clinical aspects characteristic of the

ulcerative phase seen through macroscopic and microscopic scores, faithfully mimicking the findings identified in the oncology clinic in patients undergoing chemotherapy by 5-FU.

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