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Abstract

Photoprotective and Therapeutic Potential in Skin Cancer of Amaryllidaceae Alkaloids †

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Skin cancer has evolved as the most common malignant disease, accounting for 4.5% of all new cancer cases. Melanoma, the most aggressive skin cancer type, develops in melanocytes and has high mortality rates due to its biological features and frequent failures of therapeutic alternatives. On the other hand, non-melanoma skin cancers (NMSC), the most common malignant tumors in humans, are developed in keratinocytes of the basal or spinous layer, and increased exposure to ultraviolet (UV) light remains the most important modifiable risk factor. To date, treatment alternatives for melanoma are limited to surgery, in cases of early diagnosis, and a few pharmacological options in inoperable tumors. These limitations for skin cancer management evidence the need to develop therapeutic options for prevention and treatment. The antiproliferative effects of Amaryllidaceae alkaloids have been tested for different types of cancer. However, their activity on skin models is not well-established. Pure alkaloids and alkaloidal fractions characterized by GC-MS of several Amaryllidaceae species from *Crinum*, *Zephyranthes*, *Hippeastrum*, and *Eucharis* genera were assayed by their effects on skin cancer. Photoprotective effects of the alkaloids and fractions were determined through cell viability assay, and the quantification of intracellular reactive oxygen species (ROS) and inflammation biomarker IL-6 in UVB-stimulated keratinocytes (HaCaT). Cytotoxicity were assessed in human metastatic melanoma cells (CRL-3229) to evaluate therapeutic potential, and chemometric techniques were used to analyze data. Most substances enhanced HaCaT proliferation at 5.0 µg/mL. *E. caucana* and *Z. carinata* bulbs alkaloidal fractions significantly reduced intracellular ROS and IL-6 production in UVB-stimulated HaCaT, respectively. Tazettine and lycoramine showed photoprotective effects. Additionally, *E. caucana* bulbs alkaloidal fraction was selectively cytotoxic in melanoma cells at 20.0 µg/mL. Collectively, these results demonstrate that Amaryllidaceae alkaloids could represent a new option in skin cancer management, acting as photoprotective agents in healthy UVB-exposed keratinocytes and therapeutic agents in melanoma.