Mechanism of Riboflavin Phototoxicity Based on Inflammation, senescence and Apoptosis Markers: Potential Application on Photodynamic Therapy

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Riboflavin (RF) belongs to B_2 vitamin complex and besides being a precursor of FMN and FAD coenzymes, RF presents important biological properties such as antitumoral and photosensitizing activities. The main goals of this work were to evaluate the riboflavin phototoxicity in human keratinocytes (HaCaT) and fibroblasts (BALB/c 3T3), as well as to identify molecular markers of inflammation, senescence and cellular death responses towards chemical and physical damages. Our results indicated that low concentrations of RF display photoprotective action towards UVA. However, at higher concentrations of RF (5 - 6 μM) and 5 J/cm^2 dose of UVA we observed caspases activation which indicates apoptosis induction. In addition, increased phospho-caveolin levels in both cell lines and p21 in HaCaT cells can be associated with the cellular cycle arrest. Our findings also revealed that RF in presence of UVA induces precocious senescence process as indicated by the increase of metalloproteinases 2 and 9 (MMP2 and 9). The examination of NFκB and phospho-IKKα/β levels indicated that RF does not change the inflammation process unchained by UVA in BALB/c 3T3 cells. On the other hand, in HaCaT cells the inflammation process was activated. Our data demonstrated that RF, under UVA irradiation, can lead cells to apoptosis, inflammation and precocious senescence processes. Therefore, RF might present a great application in photodynamic therapy, once it showed phototoxicity when irradiated with sub-toxic doses of UVA.

Key words: riboflavin, phototoxicity, Inflammation, senescence and apoptosis Markers, photodynamic therapy

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