NOVEL FLUORESCENT MITOCHONDRIAL-TARGETING LIPOSOMAL DRUG-DELIVERY SYSTEM OF Ga(III)-NARINGENIN COMPLEX FOR ANTICANCER APPLICATIONS

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ABSTRACT

Delivery of pharmacologically active molecules into individual subcellular compartments, such as mitochondria, is a must for achieving enhanced therapeutic activity compared with traditional random intracellular distribution.[1] Phospholipid vesicles (liposomes) containing anticancer agents produce fewer side effects than non-liposomal anticancer formulations, while functionalization of their surface plays a key role in the targeting of solid tumours.[2] Flavonoids are among the most investigated phytochemicals due to their wide spectrum of pharmacological activities. Their action is strongly related to their ability to form complexes with transition metal ions of biological interest, generating novel metallodrugs with therapeutic potential.[3] In view of the above, in this work, a novel fluorescent, mitochondrial-targeting liposomal drug-delivery system was prepared through the employment of a surface modified DSPE-PEG-aldehyde (DSPE-PEG-CHO) phospholipid with the mitochondriotropic dye rhodamine-123 (Rh123). The produced liposomal formulations were used as nanocarriers of a novel Ga(III) complex of naringenin, a bioactive flavonoid with well-established antioxidant and anticancer activity. Both the Ga(III)-naringenin complex and the generated liposomal formulations, were physico-chemically and structurally characterized with several techniques. For the investigation of anticancer properties, *in vitro* biological evaluation of the Ga-naringenin complex in its free and encapsulated form is currently taking place in breast and prostate cancer cell lines, with promising results.

KEYWORDS: Flavonoids, Metallodrugs, Liposomes, Drug-delivery, Anticancer

REFERENCES

[1] Szabo I, Zoratti M, Biasutto L. (2021). *Redox Biol.,* 42, 101846.

[2] Nel J, Elkhoury K, Velot É, Bianchi A, Acherar S, Francius G, Tamayol A, Grandemange S. (2023). *Bioact. Mater.,* 24, 401-437.

[3] Selvaraj S, Krishnaswamy S, Devashya V, Sethuraman S, Krishnan UM. (2014). *Med. Res. Rev.*, 34, 677-702.