ABSTRACT

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Title: Defining the anti-cancer role and elucidating the mechanism behind the selective anti-cancer ability of the plant derived flavonoid eriodictyol.

Submitted by: Shibjyoti Debnath

Anti-inflammatory flavonoid Eriodictyol displays selective cytotoxicity towards cancer cells compared to normal cells. Investigation of this phenomenon at the molecular level revealed that Eriodictyol significantly upregulated TNFR1 expression in tumor cells (HeLa and SK-RC-45) while normal cells (HEK and NKE) displayed negligible TNFR1 expression irrespective of absence or presence of Eriodictyol. Detailed mechanistic study revealed that Eriodictyol induced apoptosis through expression of the pro-apoptotic components, namely TNFR1, FADD and TRADD in cancer cells. In addition, CRISPR/Cas9 mediated knockout of TNFR1 was also found to completely abrogate apoptosis in HeLa cells in response to Eriodictyol. Finally, *in vivo* data demonstrated that Eriodictyol impedes tumor growth, progression and metastasis in mice implanted with 4T1 breast cancer cells. Thus, our study has identified Eriodictyol as a compound with high selectivity index towards cancer cells through a novel anti-tumor mechanism and suggest that it can be further explored for its potential to be used in cancer therapeutics.

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The thesis has been divided into three chapters -

Chapter 1 Screening and identification of anti-inflammatory polyphenols as potent anti-cancer agents-Identification of Eriodictyol as a selective cytotoxic agent.

Chapter Defining the anti-cancer role of Eriodictyol, and delineating the mechanism of its selective cytotoxicity.

Chapter 3 Assessment of the role of Eriodictyol in prevention of cancer progression and metastasis in *in vivo* syngeneic mice tumour model.

Therefore, my research work dissected *the detailed molecular mechanism behind the selective cytotoxicity of Eriodictyol towards cancer cell lines. We have shown how TNFR1 plays an important role in Eriodictyol mediated apoptosis selectively in cancer cells.*

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