

## **In Vivo Antitumor And Antimetastatic Effects Of Flavokawain B In 4t1 Breast Cancer Cell-Challenged Mice**

Nadiah Abu<sup>a,b</sup>, Nurul Elyani Mohamed<sup>b</sup>, Swee Keong Yeap<sup>c</sup>, Kian Lam Lim<sup>d</sup>, M Nadeem Akhtar<sup>e</sup>, Aimi Jamil Zulfadli<sup>c</sup>, Beh Boon Kee<sup>b</sup>, Mohd Puad Abdullah<sup>b</sup>, Abdul Rahman Omar<sup>c</sup>, and Noorjahan Banu Alitheen<sup>b</sup>

<sup>a</sup>Bright Sparks Unit, Universiti Malaya, Kuala Lumpur, Malaysia

<sup>b</sup>Department of Cell and Molecular Biology, Faculty of Biotechnology and Biomolecular Sciences, Universiti Putra Malaysia, Serdang, Selangor Darul Ehsan, Malaysia

<sup>c</sup>Institute of Bioscience, Universiti Putra Malaysia, Serdang, Selangor Darul Ehsan, Malaysia

<sup>d</sup>Faculty of Medicine and Health Sciences, Universiti Tunku Abdul Rahman, Lot PT, Jalan Sungai Long, Bandar Sungai Long, Cheras, Selangor, Malaysia

<sup>e</sup>Faculty of Industrial Sciences and Technology, Universiti Malaysia Pahang, Lebuhraya Tun Razak, Kuantan Pahang, Malaysia

<sup>e</sup>Faculty of Industrial Sciences and Technology, Universiti Malaysia Pahang, Lebuhraya Tun Razak, Kuantan Pahang, Malaysia

### **ABSTRACT**

Flavokawain B (FKB) is a naturally occurring chalcone that can be isolated through the root extracts of the kava-kava plant (*Piper methysticum*). It can also be synthesized chemically to increase the yield. This compound is a promising candidate as a biological agent, as it is reported to be involved in a wide range of biological activities. Furthermore, FKB was reported to have antitumorigenic effects in several cancer cell lines in vitro. However, the in vivo antitumor effects of FKB have not been reported on yet. Breast cancer is one of the major causes of cancer-related deaths in the world today. Any potential treatment should not only impede the growth of the tumor, but also modulate the immune system efficiently and inhibit the formation of secondary tumors. As presented in our study, FKB induced apoptosis in 4T1 tumors in vivo, as evidenced by the terminal deoxynucleotidyl transferase dUTP nick end labeling and hematoxylin and eosin staining of the tumor. FKB also regulated the immune system by increasing both helper and cytolytic T-cell and natural killer cell populations. In addition, FKB also enhanced the levels of interleukin 2 and interferon gamma but suppressed interleukin 1B. Apart from that, FKB was also found to inhibit metastasis, as evaluated by clonogenic assay, bone marrow smearing assay, real-time polymerase chain reaction, Western blot, and proteome profiler analysis. All in all, FKB may serve as a promising anticancer agent, especially in treating breast cancer.

**KEYWORDS:** flavokawain B, kava-kava, 4T1, cancer, metastasis

**DOI: 10.2147/DDDT.S67976**