UNIVERSITI TEKNOLOGI MARA

CYTOTOXIC EFFECT OF SYNTHETIC STILBENES AGAINST BREAST, COLON AND LUNG CANCER CELL LINES

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AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the result of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any other degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

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ABSTRACT

The struggle to fight and find a cure for cancer has been discussed and researched widely. The rise in cancers incidents has also caused an increase in economic burden. Various methods to treat cancer have been developed but one of the most efficient ways is through chemotherapy. The source of chemotherapy drugs includes natural products and synthetic compounds. Nevertheless, advanced technology has made synthetic drugs more attractive as compared to natural products. In the present study, 12 synthetic stilbenes (**S1 - S12**) were investigated for their potential as anticancer drugs. These stilbenes were tested for cytotoxicity against the human breast (MDA231, MDA468 and T47D), colon (HCT116 and HT29) and lung (A549) cancer cell lines and non-cancerous (WRL68, MRC-5 and FHC) cell lines. From the cytotoxic test, eight active stilbenes (**S1**, **S2**, **S3**, **S4**, **S6**, **S8**, **S9** and **S11**) with $IC_{50} \leq 10$ μM were identified. For further studies, their selectivity towards cancer and non-cancerous cell lines were also determined. Apoptosis was then investigated using; Cell Death Detection ELISA^{PLUS} (Roche kit) in 72 hour and for flowcytometry using Annexin V with Propidium iodide (PI) at four different time points (12 h, 24 h, 48 h and 72 h). The Cell Death Assay and Flowcytometry results showed that all the active stilbenes kill cancer cells mostly through apoptosis. All stilbenes were optimized synthetically in Heck reaction, where the percentages of increased yields were noted. From the eight active stilbenes, only three stilbenes (**S2**, **S8** & **S11**) were produced in higher yield compared to a previous study. *In vivo* acute toxicity studies and all the active stilbenes was conducted using balb/c mice. No significant difference in body weight and food intake changes in both female and male mice was observed. The high dose was 200 mg/kg and low dose was 100 mg/kg. For histology, the mice's organs of liver, spleen, heart, colon, kidney and lung were observed. All mice survived from the doses except for group **S3HD**, **S6LD**, **S6HD**, **S11LD** and **S11LD** had showed toxicity where mild lesion can be seen inside the histology of spleen and lung but still considered normal, therefore all active stilbenes were safe in doses up to 200 mg/kg.

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