

**AN INVESTIGATION INTO POSSIBLE APOPTOTIC  
ACTIVITY OF FLUVASTATIN ON HUMAN PROSTATE  
ADENOCARCINOMA**

A Thesis

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**ABSTRACT****An investigation into possible apoptotic activity of fluvastatin on human  
prostate adenocarcinoma****Christopher Stephen George Murray**

Apoptosis is a mechanism by which many chemotherapeutic agents exert their pharmacological action upon malignant cells, resulting in tumour regression and leading to an improvement in the health of the patient. Much research is geared at finding ways and means to employ this mechanism with the anticipation that discovery of therapeutic value in novel or existing agents will add new options to the current drugs of choice for the treatment of cancer.

In this thesis, the effect of the hypolipidemic pharmaceutical drug, fluvastatin, upon the cells of both malignant and benign human prostatic tissues, using molecular pharmacological assays *in vitro*, was examined for apoptotic activity. Three molecular assays were performed, which measured levels of caspase-3, cytochrome c, and the frequency of DNA strand breaks by light microscopy in both malignant and benign treated and untreated cells. This was followed by application *in vivo* using malignant human subcutaneous prostate xenografts in an immunosuppressed rat model.

*In vitro* tests for caspase-3 and cytochrome c showed mild apoptotic activity in the cells of malignant biopsies treated with fluvastatin in comparison to untreated and

benign controls. The light microscopy tests also indicated DNA strand breaks, typical of apoptotic cleavage, in the treated cells.

Serial human serum prostate-specific antigen tests which were conducted before and during administration of fluvastatin to the animals showed that the drug had significant effects on the level of the human serum prostate-specific antigen expressed, but not on the extent of survival of the hosts.

It is therefore concluded that fluvastatin exhibited a very mild apoptotic effect on malignant prostatic cells *in vitro*, but this effect was not demonstrable *in vivo* in a mammalian cancer model.

**Key Words:** apoptosis; prostate cancer; fluvastatin; caspase-3; cytochrome c; xenograft; DNA strand breaks, prostate-specific antigen