

IDENTIFICATION OF OESTRONE SULPHATASE INHIBITORS IN BREAST CYST FLUID: A NEW TREATMENT FOR BREAST CANCER

L.C. Lai

Faculty of Medicine and Health Sciences
Universiti Putra Malaysia, 43400 UPM, Serdang, Selangor,
Malaysia

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Introduction

Oestrogens play an important role in the development of breast cancer. Oestrone sulphate is a major source of active oestrogens in the breast, being converted to oestrone by oestrone sulphatase. Oestrone is then converted to oestradiol, a potent oestrogen strongly implicated in the development of breast cancer, by the enzyme 17 β -hydroxysteroid dehydrogenase. In vitro oestrone sulphatase activity in breast tissue has been shown to be at least 1,000 times as high as aromatase activity, which converts androgens to oestrogens. Hence, local production of active oestrogens from oestrone sulphate is a very important source of oestrogens in breast tumours. I have previously found that breast cyst fluid is a potent inhibitor of oestrone sulphatase activity in certain breast cancer cell lines. Oestrone sulphatase inhibition is potentially of great importance in the treatment of women with hormone-dependent breast cancers. The aim of this study was to identify the substances present in breast cyst fluid which are responsible for the oestrone sulphatase inhibitory property of breast cyst fluid.

Materials and Methods

Breast cyst fluid was obtained by needle aspiration of palpable breast cysts from women attending the Breast Clinic at Universiti Hospital, Kuala Lumpur, under the care of Associate Professor Dr. Yip Cheng Har. The samples were centrifuged and the supernatant stored at -20°C until assayed. High performance liquid chromatography will be carried out to separate substances according to molecular weight and fractions which are found to inhibit oestrone sulphatase ac-

tivity in breast cancer cell lines will be subjected to sodium dodecyl sulphate-polyacrylamide gel electrophoresis. Electrophoresis on to nitrocellulose were carried out and proteins responsible for oestrone sulphatase inhibition were identified by N-terminal amino acid sequencing. The procedure for MCF-7 and MDA-MB-231 cell culture as well as the oestrone sulphatase assay have been described (Erbas et al. 1996)

Results and Discussion

This study is due to be completed at the end of the year 2000. Hence, the results described here are results, which have been obtained, in the first year of the study. Our preliminary studies have shown that, unlike Western women where breast cyst fluid inhibits oestrone sulphatase activity in the MCF-7 hormone-dependent breast cancer cell line and stimulates oestrone sulphatase activity in the MBA-MD-231 hormone-independent breast cancer cell line, in our Malaysian population breast cyst fluid stimulates oestrone sulphatase activity in the MCF-7 cell line and inhibits oestrone sulphatase activity in the MDA-MB-231 cell line. This difference between Western and Malaysian females could be due the differences in the proportions of the many constituents present in the breast cyst fluid of the two female populations. The oestrone sulphatase inhibitory property of breast cyst fluid is non-dialysable, using a dialysis membrane with a molecular weight cut-off of 3,500 daltons, implying that this property of breast cyst fluid is due to a high molecular weight substance. The ability of breast cyst fluid to inhibit oestrone sulphatase activity is retained after heat treatment for 60 minutes at 65°C, implying that the substance(s) involved are heat stable. Work is now being conducted to identify the substances responsible for the oestrone sulphatase inhibitory property of breast cyst fluid.

Conclusions

The oestrone sulphatase inhibitory property of breast cyst fluid is due to one or more high molecular weight substances.

References

- Erbas, H., Lennard, T.W.J. and Lai, L.C. 1996. Effect of breast cyst fluid on oestrone sulphatase activity in MCF-7 breast cancer cells, *Anticancer Research*. 16: 833-836.