

## MASTER'S THESIS

### Measuring the binding kinetics of estrogen receptor alpha and dietary estrogens

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## Abstract

Anti-estrogen drugs such as Tamoxifen and Raloxifene are widely prescribed for breast cancer patients. While they are effective, they also have serious side effects. Alternative drugs are therefore being developed. In the drug discovery process, the *in vitro* binding of estrogen receptors and lead compounds were studied. The binding strength was conventionally quantified in terms of equilibrium dissociation constants ( $K_D$ ). However, the binding kinetic rates and especially off-rates ( $k_{off}$ ) were recently shown to be better indicators of drug potency. In this thesis, we identified a few dietary estrogens as candidate lead compounds. We studied the binding of full-length human recombinant ER $\alpha$  with these dietary estrogens. In particular, we measured for the first time their binding kinetics rate constants. We also measured the change in the receptor-ligand binding kinetics upon its recruitment of co-activators, as a means to gauge agonist/antagonist propensity of the ligand. Our results showed that the following dietary estrogens,  $\alpha$ -Zearalenol, Zearalenone, and Coumestrol bind favorably to the estrogen receptor alpha.

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