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Inhibition of 17β hydroxysteroid dehydrogenases from phytoestrogens: a combined kinetic and structural approach

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Steroid hormones act via specific receptors that activate gene transcription; hydroxysteroid dehydrogenases (HSDs) are responsible for pre-receptor regulation of steroid hormone activity. Indeed, 17β hydroxysteroid dehydrogenase (17β-HSD) modulate the biological potency of estrogens and androgens by reducing the (inactive) keto-form or oxidizing the (active) hydroxy-form at C17.
17β-HSDs are widespread among all organism, from vertebrates to bacteria. In humans, several different 17β-HSDs have been identified that are related to the development of pathologies such as breast and prostate cancers, Alzheimer's disease, polycystic kidney disease.
17β-HSD from the filamentous fungus Cochliobolus lunatus (17β-HSDcl) is the first, fully characterized fungal HSD. Its role in fungal metabolism is still not fully understood and recently it has been linked to the biosynthetic pathway leading to citoskyrin A, a potent in-vitro antibacterial. 17β-HSDcl has been proposed as a useful model system when studying the function of HSD enzymes belonging to the Short Chain Dehydrogenases superfamily. Indeed, by linking kinetics and structural data we have been trying to relate the structure and the function of 17β-HSDcl. Besides, by following the same approach we have investigated the inhibitory action of selected flavonols and isoflavones, which are known modulators of the endocrine system, in order to elucidate the structural determinants of their inhibitory action.

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