# ENZYME/PRODRUG SYSTEMS FOR CANCER TREATMENT

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Fluorouracil is a chemotherapy drug used to treat different cancers including breast, skin, stomach, pancreatic, bowel. However, at its therapeutic dose it causes significant side effects such as mucositis, myelosuppression, dermatitis, and cardial toxicity [1]. Due to these side effects, its application as prodrug in the form of fluorocytosine in combination with cytosine deaminase has gained attention in the past decades. The cytosine deaminase/5-fluorocytosine system is among the best explored enzyme/prodrug systems for cancer therapy [2]. In this system, 5-fluorocytosine, non-toxic prodrug, is converted to its active form 5-fluorouracil by cytosine deaminase activity. The use of this system has some drawbacks, such as the non-specific targeting of normal cells that are located in the vicinity of the tumor [3] and also the deleterious effects of 5-fluorocytosine to the organism ranging from minor side effects such as nausea, vomiting and diarrhea to serious ill-effects such as hepatotoxicity and bone-marrow depression have been reported in a number of clinical studies [4]. Recently, a new 5-fluoroisocytosine/isocytosine deaminase system has been proposed. This novel enzyme/prodrug pair alleviates the toxic side effects, and could be used as an improved the cancer therapy [5,6].

In this study, new promising enzyme/prodrug systems were investigated. We synthesized novel 5-fluorocytosine/isocytosine and uridine acylated derivatives as possible prodrugs and tested the ability of hydrolases to convert these compounds into the drug 5-fluorouracil (Fig. 1).

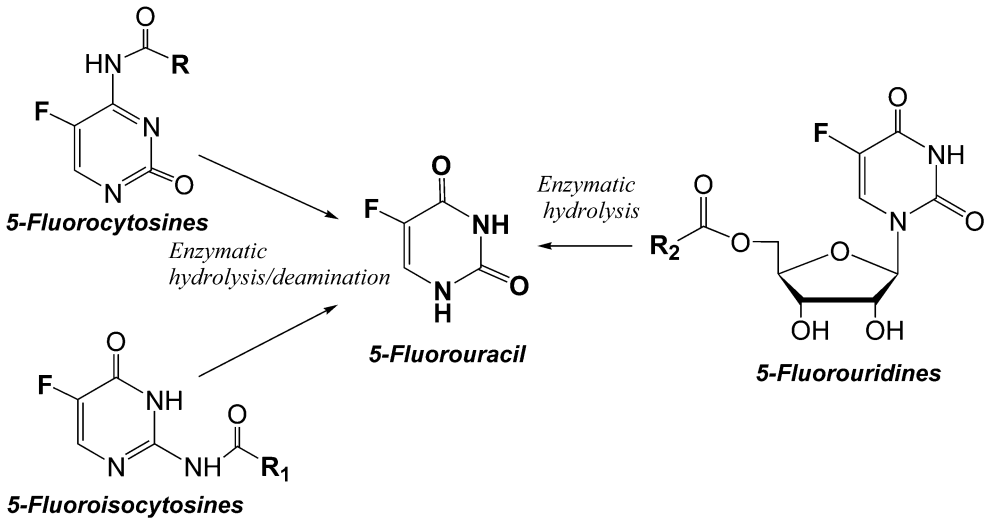


Fig. 1. Enzymatic conversion of inactive prodrugs into toxic drug 5-fluorouracil.

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