МЕДИЦИНСКИ УНИВЕРСИТЕТ - ВАРНА
„Проф. д-р Параскев Стоянов“
Ул.“Марин Дринов“ 55, Варна 9002, България
Тел. : 052/ 65 00 57, Факс: 052/ 65 00 19
e-mail: uni@mu-varna.bg, www.mu-varna.bg

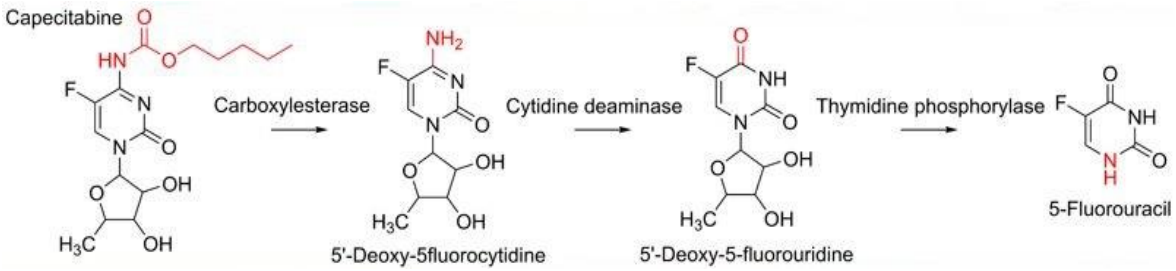
MEDICAL UNIVERSITY - VARNA
“Prof. Dr. Paraskev Stoyanov”
55, Marin Drinov Str., 9002 Varna, Bulgaria
Tel.: +359 52/ 65 00 57, Fax: + 359 52/ 65 00 19
e-mail: uni@mu-varna.bg, www.mu-varna.bg

Fund “Nauka” Project № 19029 Resume

“Study of the effect of specific carboxylesterase inhibitors on the effectiveness of chemotherapy with Capecitabine”

Project leader: Prof. Petko Marinov, MD, PhD

Capecitabine is an antineoplastic *pro-drug*, representative of the fluoropyrimidine



class. Once administered, the *pro-drug* is, *in vivo*, metabolised by a triad of enzymes into its active form (metabolite) - *5-Fluorouracil* (Fig. 1).

Figure 1. Three-step activation of Capecitabine

Both *5-Fluorouracil* and *Capecitabine* have been traditionally used in the treatment of multiple malignancies for years. Unlike *5-Fluorouracil*, however, *Capecitabine* is currently considered as a chemotherapeutic agent of first choice. Indeed, the clinical outcomes of *Capecitabine* treatment in terms of efficacy and side effects are more than acceptable.

A review of the medical literature has, however, shown that the number of studies related to enhancement of the *Capecitabine’s* theraupetic index is too limited.

The main strategies concern: the combination of *Capecitabine* with calcium folinate; the use of selective aminopeptidase-N (CD13; genomic) and dUTPase / DPD inhibitors, as well as the use of nanostructured materials for drug delivery.

On the othe hand, the crucial role of several genetic alterations on *Capecitabine’s* theraupetic effciency has also been reported in several isolated reports. In this regard, the established relationships between CES2 and CES1 genes polymorphisms and the activity of the *pro-drug* in question have been considered as extremely intriguing.

These genes are known to affect the expression of CES2 and CES1 enzymes, responsible for the first stage of *Capecitabine* metabolism.

For the time being, however, there is no information about the activity of CES-inhibitors and their influence on the bioavailability of *Capecitabine*.

All these findings and questions highlightted the relevance of the present study,

namely: To determine the effect of various CES inhibitors on the bioavailability of *Capecitabine* and its efficacy in the treatment of malignant tumors.

For the aim: The chemotherapeutic (antitumor) efficacy of *Capecitabine* in combination with CES-inhibitors was evaluated against Icr Albino Mice inoculated with Ehrlich-Lettre ascites cells.

The main aim of this study is: To generate of an innovative therapeutic approach/strategy for malignant tumors therapy – an approach bearing the traces of the modern pharmacological, phyto-, and nutritional therapy.

The current research can be viewed as interdisciplinary and focused on the priority scientific area - oncology and rare diseases.