Drug report: Capecitabine

By: Zara Islam
Course: CHEM 3071

Introduction

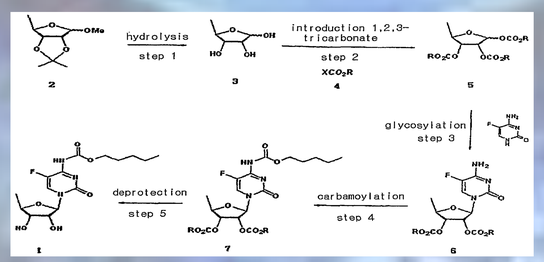
Capecitabine is a known orally-administered chemotherapeutic agent which is employed in the treatment of metastatic, breast and colorectal cancers. It the brand name Xeloda

History

In 1986, scientists discovered prodrug doxifluridine but due to the toxicity effect scientists tried to synthesize a unique fluoropyrimidine characterized by improved efficacy and safety profiles .These studies lead the scientists to discover the drug capecitabine (Ishikawa et al. 1998).

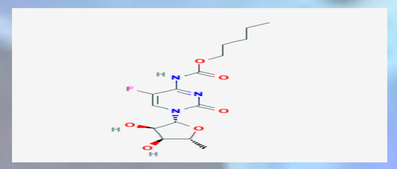
Synthesis

The most widely used process of synthesis of capecitabine is with D-ribose (Soni 1987).
Another way to synthesize capecitabine was a three step process with the starting material being 5- fluorocytosine (Ishitsuka and Shimma 1997)



Molecular Structure

The molecular formula if this drug is C15H22FN3O6 (Ishitsuka, and Shimma 2010). The chemical name for capecitabine is 5'-deoxy-5-fluoro-N-[(pentyloxy) carbonyl]-cytidine. it's a relative molecular mass of 359.35 g/mol. (Lobb et al. 2004)



Dosage

Capecitabine requires a repeated cumulative dosage over a prolonged period of time to show positive effects. The doses are provided orally. There are limited numbers of dosage given according to patients condition.

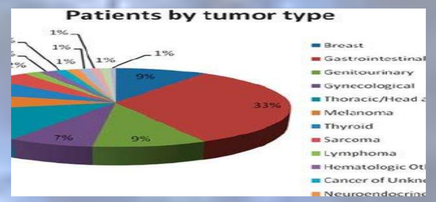
Table 1 XELODA Dose Calculation According to Body Surface Area

Dose Level 1250 mg/m² Twice a Day		Number of Tablets to be Taken at Each Dose (Morning and Evening)	
Surface Area (m^2)	Total Daily Dose* (mg)	150 mg	500 mg
≤ 1.25	3000	0	3
1.26-1.37	3300	1	3
1.38-1.51	3600	2	3
1.52-1.65	4000	0	4
1.66-1.77	4300	1	4
1.78-1.91	4600	2	4
1.92-2.05	5000	0	5
2.06-2.17	5300	1	5
≥ 2.18	5600	2	5

* Total Daily Dose divided by 2 to allow equal morning and evening doses

Toxicity

The oral lethal dose was determined to be > 2000 mg/kg and the maximum non-lethal intravenous dose was determined to be > 250 mg/kg for males and >375 but < 500 mg/kg for females (Gilani and Giridharan 2014).

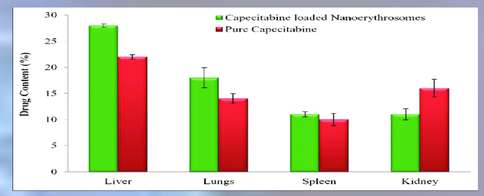


Absorption

It is readily absorbed through the GI tract. The first-pass effect in the liver plays a major role in the bioavailability of capecitabine and metabolites (Herr 2010).

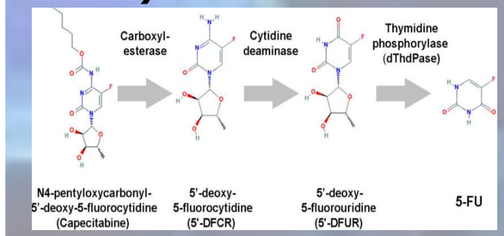
Distribution

Capecitabine is primarily bound to human albumin protein which is produced in the liver. Albumin protein is responsible for the transportation of the drug molecules (Uno 1993)



Metabolism

Capecitabine has a half life of 45-60 minutes Capecitabine gets transformed to 5-fluorouracil by three enzymes which are located in the liver and tumors (Vaccaro et al. 2008).



Excretion

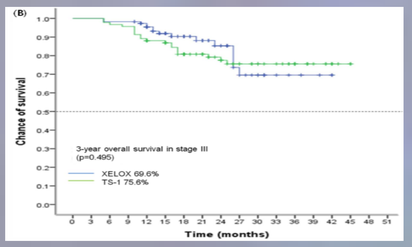
Capecitabine and its metabolites mostly get excreted in urine. Fecal excretion is very low. Almost 95% of administered capecitabine dose can be recovered in urine (Ciceri et al. 2015).

Side Effects

Even though this drug s a very good chemotherapeutic it has some side effect

Comparison with other drugs

There is another drug called oxaliplatin which works similarly to capecitabine. Oxaliplatin is given to the patient through injection so it has a higher chance of overdose.
Also, the success rate of oxaliplatin is less than capecitabine (Cunningham 2012).



Conclusion

Capecitabine is a drug that has been approved by the FDA to be used as first-line therapy in patients who have metastatic colorectal cancer (Reigner et al. 2001).. More research is being done on this drug to improve its dosage length but till today Capecitabine is considered one of the best chemotherapeutic drug.