INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Article

Review on Theoretical Study of Capecitabine Use in Colon Cancer

Neha Ramhari Pawar*

Yashodeep Institute of Pharmacy.

ARTICLE INFO

Published: 06 June 2025
Keywords:
Study of Capecitabine, pharmacodynamics, pharmacokinetics, clinical efficacy, and toxicity profile
DOI:
10.5281/zenodo.15609049

ABSTRACT

Capecitabine, an oral prodrug of 5-fluorouracil (5-FU), has emerged as a cornerstone in the chemotherapeutic management of colon cancer, particularly in adjuvant and metastatic settings. This theoretical review explores the pharmacodynamics, pharmacokinetics, clinical efficacy, and toxicity profile of capecitabine in colon cancer treatment. The drug's tumor-selective activation via thymidine phosphorylase and its oral administration confers potential advantages regarding patient convenience and quality of life. Clinical studies have demonstrated comparable efficacy between capecitabine and intravenous 5-FU regimens, with varying toxicity profiles. Furthermore, this review examines the molecular basis of capecitabine's action, resistance mechanisms, and potential for combination therapy with targeted agents. By synthesizing current literature and theoretical frameworks, this review aims to provide a deeper understanding of capecitabine's role in colorectal cancer therapy and inform future directions in personalized oncology.

INTRODUCTION

Colon cancer remains one of the leading causes of cancer-related morbidity and mortality worldwide. Chemotherapy is pivotal in its management, especially in the adjuvant and metastatic settings. Among the chemotherapeutic agents, capecitabine, an oral fluoropyrimidine carbamate, has become a prodrug that is enzymatically converted into 5-fluorouracil (5-FU) within tumor tissues. This targeted activation allows for tumor-selective cytotoxicity, potentially improving therapeutic outcomes while reducing systemic toxicity. Capecitabine offers several advantages over traditional intravenous 5-FU, including ease of administration, reduced need for hospital visits, and improved patient compliance. The theoretical framework supporting capecitabine's use includes its pharmacokinetic and pharmacodynamic properties, tumor-selective activation mechanisms, and synergy with other agents such as oxaliplatin or bevacizumab. This review aims to critically examine the theoretical basis for

***Corresponding Author:** Neha Ramhari Pawar
Address: *Yashodeep Institute of Pharmacy.*
Email ✉: neharpawar123@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

capecitabine's role in colon cancer treatment. It explores the drug's molecular mechanism, patterns of resistance, and its integration into various treatment protocols. By understanding these theoretical underpinnings, we can better appreciate capecitabine's potential in enhancing therapeutic outcomes in colon cancer patients.

Stomach Cancer or Intestinal Cancer

The stomach: -

The stomach is a sac-like organ that's an important part of the digestive system. After the food is chewed and swallowed, it can enter the esophagus, a tube that carries food through the throat and chest to the stomach. The esophagus joins the stomach at the gastroesophageal (GE) junction, which is just beneath the diaphragm (the thin sheet of breathing muscle under the lungs). The Stomach then starts to digest the food by secreting digestive juice. The food and gastric juice are mixed and then broken down into the first part of the small intestine, called the duodenum.

Stomach Cancer can be different from other cancers that can occur in the abdomen, like cancer of the following,

A) Colon or Rectum, large intestine
B) Liver, Pancreas
C) Small Intestine

These cancers can have different symptoms, different looks, and Different treatments.

Development Of Stomach Cancer:-

- Stomach cancer tends to develop slowly over many years before a true cancer develops, Pre––
- Cancer occurs in the lining of the stomach
- Chemotherapy drug used to treat colorectal cancer (colon Cancer)

1. 5- Fluorouracil (5-fu)
2. Capecitubine
3. Irinotecan (Cumptosar) A)

1] 5- Fluorouracil PH

A clear colorless solution with a PH in the range of 8.6 to 9.4, fluorouracil should be administered only under the supervision of a qualified physician with extensive experience in cytotoxic treatment patient must be cone completely and frequently monitored during the treatment.

2] 5- Fluorouracil mode of action

5-Fu can activate P53 by more than one mechanism incorporation of fluorouracil triphosphate (FUTP) into RNA and the inhibition of thymidylate synthase (TS) by fluorodeoxyuridine monophosphate (FDUMP) with resulting in DNA damage.

3] C Dissolves

5- Fluorouracil is soluble in 1N NH4OH, which yields a clear colorless to light yellow solution. The product is also soluble in Danso (10/50mg/ml).

B)

1] Capecitabine PH: -

Assuming that capecitabine is a weak acid, 11,12 with a pKa of 8.8, theoretically it should be minimally ionized at the normal fasting gastric PH (1.3 to 1.7)

2] Capecitabine mode of action:-

Capecitabine is relatively non-cytotoxic in vitro. This drug is enzymatically converted to 5-Fluorouracil in vivo. Both normally and tumor cell metabolize 5–fu to 5fluro-2 deoxyuridine

monophosphate (FDUMP) and 5- Fluorouridine triphosphate (FUTP).

3] Capecitabine Dissolve :-

They may suggest that you dissolve the capecitabine tablet in water. In this case, dissolve the tablet in a 200 ml glass of warm water. Stir the water with a spoon until the tablet completely dissolves, and then drink it immediately.

C)

1] Ironotecan – PH

Each milliliter of solution contains 20 mg of irinotecan hydrochloride (based on) 45 g of sorbitol NF powder and 0.9 g of lactic acid. The PH of the solution has been adjusted to 3.5 with sodium hydroxide or hydrochloric acid.

2] Irinotecan mode of action

It is a derivative of camptothecin that inhibits the action of topoisomerase I. Irinotecan prevents relingation of the DNA strand by binding to topoisomerase I-DNA complex and causes double-strand DNA breakage and cell death. It is a derivative of Comptothecin.

3] Irinotecan Dissolve

For maximum solubility in acquiesce buffer, irinotecan (hydrochloride hydrate) should first be dissolved in DMSO and then diluted with the acquiesce buffer of choice. Irinotecan has a solubility of approximately 0.5 mg/ml in a 1:1 solution of DMSO: PBS (pH 7.2) using these methods [1]

❖ **Stomach Cancer / Intestinal Cancer**

Capecitabine: - (500mg)

- Packaging Size: 10 Tablet Strip
- Composition Capecitabine 500mg
- Manufacture Cipla
- Treatment of Breast Cancer and Cancer of the Colon and Rectum
- Prescription/Non Prescription
- Capegar d 500mg 1200/- Tablets 10. Price
- Capegard and Xeloda Capecitabine (500mg) (Xeloda, Capegard), Prescription, Cipla [2]

 # Capecitabine: - (500mg) Film-Coated tablets:

- Qualitative and Quantitative composition: Each film-coated tablet contains 500mg of Capecitabine.
- Excipient with known Effect: Each film-coated tablet contains 25.470mg anhydrous lactose.
- Film-coated tablet dissolution time:- Soluble tablets are un coated or film be coated tablets that are intended to be dissolve in the water giving a clear or slightly opalescent solution. Soluble tablets disintegrate with in 3 minuets when Examined by 5.3 Disintegration test for tablets and capsuies , but using water R at 15-25 ^{o}c.
- Film Coated tablets dissolution time in Stomach:- In various forms, 30 min up to 7 hr, with an average time of 6 hr. Although some studies indicate that large-sized dosage forms may require additional time for gastric emptying, others suggest that the size, shape, or volume of the tablet has no significant effect instead. [3]

 # Technique used in film-coated tablets:-

Film coating:- The process involves spraying a solution of polymer, pigment, and plasticizer onto a rotating tablet bed to form a thin, uniform film on the tablet surface. The choice of The Polymer mainly depends on the desired site of drug release (stomach/intestine) or the desired release rate.[4]

Solvent Use In Film-Coated Tablet:-

The most commonly used organic solvents are IPA and methylene chloride. Film coating of the tablets is a multivariable process, with many different factors, such as the coating equipment.[5]

Ingredient use in film-coated tablets:-

The most widely used polymers in non-functional film coating are cellulose derivatives such as hypromellose (HPMC), plasticizers used to improve the flexibility of the film formed, and prevent it from cracking or breaking. They work by weakening the attraction between the polymer molecules to make the film more malleable.[6]

PH of Film Coated Tablet:-

It is a reaction product of Phthalic anhydride, sodium acetate, and a partially hydrolyzed polyvinyl alcohol. The onset of aqueous dissolution of PVAD begins at a PH of about 5.0, allowing for enteric release as well as the potential for targeted drug release to the proximal small intestine.[7]

PH Of Sugar Bases:- (sugar solution) 7 to 7.4

Sugar, when dissolved in water, does not give or take any hydrogen ions from the water. Sugar forms a non-ionic compound, thus, it does not release H+ or OH ions in the water solution. The PH values of the sugar solution will be as that of water is 7 to 7.4. This sugar solution will always be natural.[8]

 # Natural Polymer More than 7.8 PH

1) Milk of magnesia, PH=10.5: -

With a PH greater than 7, milk of magnesia is basic. (Milk of magnesia is largely $Mg(OH)_2$)

2) **Pure water with a PH 7**

Pure water with a PH of 7 is natural

3) Wine with PH 3.0

With a pH of less than 7, wine is Acidic Identify each substance as acidic, basic, or neutral based only on the stated PH.

- Human Blood PH = 7.4 (basic)
- Household ammonia, PH=11.0 (basic)
- Cherries, PH =3.6 (acidic) [9]

Film Coating Over Sugar Coating:-

Enhances the elegance and glossy appearance of coated tablets. 3 Minimal weight increase (typically 2 - 3% of tablet core weights) as opposed to more than 50% with sugar coating.

How to Prepare Sugar Bigasess:-

1) Harvesting sugar cane and sugar beets is typically done from the fields mechanically.
2) Washing and Initial Preparation
3) Juice Extraction
4) Purification of Juice
5) Crystallization
6) Centrifugation
7) Drying and [10]

Sugar Bigasess Formulation: -

- Chemical formula $C_{12}H_{22}O_{11}$
- Molecular Weight 342.30 g/mol
- Density 1.587 g/cm^3
- Melting Point Decomposes 186 ^oc [11]

Which Kind of Drug Use of Sugar Bigasess: -

- **Flavor Balance: -** Sugar adds Sweetness and balances acidic and bitter flavors in tomato and vinegar-based sauces, dressing, and brains.

- **Preservative:** Sugar stops bacteria from growing and delays spoilage.

- **Texture and Mouthfeel:** -sugar helps provide the soft structure in baked goods and smoothness in frozen dairy products.

- **Volume:** Sugar adds volume to different products and which allows them to be tall, fluffy, or soft

- **Colour:-** Sugar reats with heat carumelization) or with heat and proteins (maillard reaction) to creat a golden brown colour in based goods and sauces.

- **Taste**:- a little bit of sugar can make high fiber food taste better [12]

 # Props Of Use:-

Medicines used to treat cancer are very strong and can have many side effects. Before using this medicine, make sure you understand all the risks and benefits. You need to work closely with your doctor during your treatment. Take this medicine exactly as directed by your doctor. Do not take more of it, do not take it more often, and do not take it for a longer time than your doctor ordered. To do so may increase the chance of side effects. This medicine should come with a patient information leaflet. Read and follow these instructions carefully. Ask your doctor if you have any questions. Take this medicine with food or within 30 minutes after you eat. Swallow the tablet whole with water. Do not cut, crush, break, or chew it. If the tablet must be cut or crushed, it should be done by a pharmacist.[13]

 # Dosing

The dose of this medicine will be different for different patients. Follow your doctor's orders or the directions on the label. The following information includes only the average doses of this medicine. If your dose is different, do not change it unless your doctor tells you to do so. The amount of medicine that you take depends on the strength of the medicine. Also, the number of doses you take each day, the time allowed between doses, and the length of time you take the medicine depend on the medical problem for which you are using the medicine.

- For oral dosage form (tablets):

  - For metastatic breast and colorectal cancer:

    - For patients receiving this medicine alone:

    - Adults—Dose is based on body size and must be determined by your doctor. At first, 2500 milligrams (mg) per square meter (m(2)) of body size per day, divided in 2 doses and taken about 12 hours apart. These doses are taken for 2 weeks, followed by 1 week rest, given as 3 weeks cycle. Your doctor may adjust your dose if needed.

    - Children—Use and dose must be determined by your doctor.

    - For patients receiving this medicine with docetaxel:

    - Adults—Dose is based on body surface and must be determined by your doctor. At first, 2500 milligrams (mg) per square meter (m(2)) of body surface area per day, divided into 2 doses and taken about 12 hours apart. These are taken for 2 weeks, followed by 1 week rest, given as 3 3-week cycles. Your doctor may adjust your dose if needed.

    - Children—Use and dose must be determined by your doctor.[14]

 # Side Effect

Along with its needed effects, a medicine may cause some unwanted effects. Although not all of these side effects may occur, if they do occur, they may need medical attention.[15]

Check with your doctor immediately if any of the following side effects occur:

More common

- Abdominal or stomach pain
- diarrhea
- Loss of fingerprints
- nausea
- numbness, pain, tingling, or other unusual sensations in the palms of the hands or bottoms of the feet
- pain, blistering, peeling, redness, or swelling of the palms of the hands or bottoms of the feet
- pain, redness, swelling, sores, or ulcers in your mouth or on your lips
- unusual tiredness or weakness
- vomiting

Less Common or Rare

- Abdominal or stomach cramping or pain (severe)
- agitation
- back pain
- bleeding and bruising
- bleeding gums
- blood in the urine or stools
- bloody nose
- Bloody or black, tarry stools
- blurred vision
- burning, dry, or itching eyes
- chest pain
- chills
- clumsiness or unsteadiness
- cold
- collapse
- coma
- confusion
- constipation
- convulsions
- cough or hoarseness (accompanied by fever or chills)
- cough producing mucus
- coughing or spitting up blood
- dark urine
- decreased frequency or amount of urine
- difficulty with breathing
- difficulty with swallowing or pain in the back of the throat or chest when swallowing
- discharge from the eyes
- drowsiness
- dry mouth
- excessive tearing
- extra heartbeats
- eye redness, irritation, or pain
- fainting
- fast or irregular heartbeat
- fever or chills
- flu-like symptoms
- hallucinations
- headache, sudden and severe
- heavier menstrual period
- high fever
- hot, red skin on the feet or legs
- Inability to speak
- increased menstrual flow or vaginal bleeding
- increased thirst
- irritability
- itching in the genital or other skin areas
- light-headedness
- light-coloured stools
- loss of consciousness
- lower back or side pain (accompanied by fever or chills)
- muscle aches or cramps
- muscle spasms
- nosebleeds
- numbness or tingling in the hands, feet, or lips

- painful or difficult urination (accompanied by fever or chills)
- painful, swollen feet or legs
- pain, tenderness, or swelling in the upper abdominal or stomach area
- pale skin
- paralysis
- pinpoint red spots on the skin
- Problems with coordination
- prolonged bleeding from cuts
- rapid, shallow breathing
- red or dark brown urine
- redness, pain, or swelling of the eye, eyelid, or inner lining of the eyelid
- scaling
- seizures
- severe constipation
- skin rash or itching
- Slow or irregular heartbeat
- slurred speech
- sneezing, sore throat, or stuffy nose
- sores, ulcers, or white spots on the lips or in the mouth
- stiff neck
- stomach bloating, burning, or cramping
- swelling of the face, fingers, feet, or lower legs
- swelling of the lymph nodes
- swollen glands
- temporary blindness
- tiredness or weakness
- trouble with speaking
- troubled breathing or tightness in the chest
- unexplained nosebleeds
- unusual bleeding or bruising
- unusual lump or swelling in the chest
- vomiting blood or material that looks like coffee grounds
- weakness in the arm or leg on one side of the body, sudden and severe
- weight gain or loss
- white patches in the mouth or throat, or on the tongue
- white patches with diaper rash
- yellow eyes or skin

CONCLUSION: -

Capecitabine-based chemotherapy regimens, especially XELOX, offer good efficacy following radical gastrectomy in Chinese patients with AGC, with a low incidence of adverse events, acceptable tolerance, greater patient convenience and a lower overall cost than other regimens. However, because of the limited data available, further clinical research with capecitabine is still necessary to establish the optimum strategy. The Committee concluded that capecitabine, in combination with a platinum-based regimen, should be recommended for the first-line treatment of inoperable advanced gastric cancer.

REFERENCES

1. www.wikipedia.org
2. https://www.medindia.net/amp/drugprice/capecitubine.htm
3. https://www.medicines.org.uk/imcl product/993915/mpc.
4. Https://www.rroij.com
5. www.Wikipedia.org
6. https://www.seppic.com/in/technologies/ film coating.
7. https://www.pharmapproach.com
8. https://saylordotorg.github.
9. https://www.ift.orglhews-and-publication/food-technology.
10. https://byjus.com/sugar-formula
11. www.The Canadian Sugar Institute. in
12. https://www.mayoclinic.org/drugs-supplements/capecitabine-oral-route/side-effects
13. https://www.mayoclinic.org/drugs-supplements/capecitabine-oral-route/side-effects

14. https://www.mskcc.org/cancer-care/patient-education/capecitabine
15. https://www.mayoclinic.org/diseases-conditions/stomach-cancer/symptoms-causes/syc-20352438.

HOW TO CITE: Neha Ramhari Pawar*, Review on Theoretical Study of Capecitabine Use in Colon Cancer, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 6, 1246-1253. https://doi.org/10.5281/zenodo.15609049