International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

A Research Paper on: Capecitabine as A Targeted Oral Anticancer Agent: Evaluation of Capecitabine (Tablet) and Therapeutic Assessment

Mr. Vishal S. Lavgale[1], Dr. Sunil S. Jaybhaye[2], Prof. Saurabh M. Bondre[3]

[1]Student, Institute of Pharmacy, Badnapur.
[2]Principal, Institute of Pharmacy, Badnapur.
[3]Assistant Professor, Institute of Pharmacy, Badnapur.

ABSTRACT:
The present research work focused on the detailed study of the oral gastro-retentive dosage forms (GRDFs) of capecitabine, including its drug profile and preformulations studies and comparison of therapeutic potential as a antineoplastic agent with the other antineoplastic agents. Marketed tablet formulations were evaluated based on various physicochemical parameters. Additionally, the therapeutic potential of capecitabine was compared with other anticancer drugs. Capecitabine, a prodrug of 5-fluorouracil (5-FU), has become a cornerstone in the treatment of various solid tumors, particularly colorectal, breast, and gastric cancers. Its unique mechanism of action involves a selective conversion into 5-FU within tumor cells through a series of metabolic steps. This targeted activation helps to minimize systemic toxicity while maximizing anticancer efficacy. Capecitabine has shown substantial effectiveness not only as a single-agent therapy but also in combination regimens, enhancing its versatility in clinical applications. Current research also focuses on identifying predictive biomarkers for better patient selection and exploring novel therapeutic combinations to improve treatment outcomes. These efforts support its potential as a personalized anticancer therapy in the era of precision medicine. In this study, the physicochemical and preformulation studies of capecitabine tablets were carried out, and the prepared formulations were evaluated thoroughly.

Keywords: Capecitabine (CPC), In vitro dissolution study, Therapeutic Potential of Capecitabine.

INTRODUCTION:

Cancer remains one of the most formidable public health challenges worldwide, affecting millions of lives and driving the continuous pursuit of more effective therapeutic strategies. Among the wide array of anticancer agents, capecitabine has established itself as a key player in the treatment of various solid tumors due to its potency and versatility.

This research provides a comprehensive overview of capecitabine, covering its pharmacological properties, clinical efficacy, safety profile, and its evolving significance in the context of precision oncology. Capecitabine is an orally administered prodrug that represents a significant advancement in

cancer pharmacotherapy. Once ingested, it is enzymatically converted into 5-fluorouracil (5-FU) within tumor tissues, leveraging the elevated expression of thymidine phosphorylase in malignant cells.
This tumor-selective activation results in a preferential cytotoxic effect on cancer cells while reducing systemic toxicity, which is often a limitation of traditional 5-FU-based treatments. This targeted mechanism underlies the widespread clinical adoption of capecitabine in the management of gastric, colorectal and breast cancers.
In 2010, approximately 12.7 million cancer cases were diagnosed globally, and about 7.6 million people died from cancer. Cancers accounted for roughly 13% of all deaths worldwide that year. The most common causes of cancer-related deaths included: lung cancer (1.3 million deaths), stomach cancer (803,000 deaths), colorectal cancer (639,000 deaths), liver cancer (610,000 deaths), and breast cancer (519,000 deaths).

STATEMENT OF PROBLEM:

Despite Capecitabine's proven efficacy as an oral antineoplastic agent, challenges remain in optimizing its therapeutic potential due to limited bioavailability, variable absorption, and gastrointestinal side effects. The development of oral gastro-retentive dosage forms (GRDFs) aims to address these limitations by enhancing drug retention and absorption in the stomach. However, comprehensive studies comparing the physicochemical properties and preformulation parameters of such GRDFs—alongside a detailed evaluation of Capecitabine's therapeutic potential relative to other anticancer agents are still lacking.
This study seeks to fill that gap by analyzing marketed formulations, conducting in-depth preformulation studies, and assessing Capecitabine's relative efficacy to support its use in personalized cancer therapy.

HYPOTHESIS:

Capecitabine-based oral gastro-retentive dosage forms (GRDFs) can enhance the therapeutic efficacy and bioavailability of the drug compared to conventional antineoplastic agents, due to its targeted activation mechanism and favourable physicochemical properties.

AIMS & OBJECTIVES:

Aims:

To conduct a comprehensive investigation of gastro-retentive dosage forms (GRDFs) of Capecitabine, focusing on its physicochemical, preformulation, and therapeutic evaluation, and to compare its efficacy with other antineoplastic agents.

Objectives:

1. To study the drug profile of Capecitabine, including its pharmacological properties and mechanism of action as a prodrug of 5-fluorouracil (5-FU).
2. To design and develop oral gastro-retentive dosage forms (GRDFs) of Capecitabine for enhanced therapeutic effect and controlled release.
3. To perform preformulation and physicochemical studies on Capecitabine to assess its compatibility, stability, and suitability for GRDF formulation.
4. To evaluate marketed tablet formulations of Capecitabine based on various physicochemical parameters such as hardness, friability, disintegration, and drug content.
5. To compare the therapeutic potential of Capecitabine with other standard antineoplastic agents in terms of efficacy, safety, and clinical versatility.

6. To explore the role of Capecitabine in personalized medicine, including the investigation of biomarkers and combination therapies for improved treatment outcomes.

PLAN OF WORK

1. Literature Review:

- Review of existing oral gastro-retentive drug delivery systems (GRDFs).
- Overview of capecitabine's pharmacokinetics, pharmacodynamics, and clinical applications.
- Comparative study of capecitabine with other antineoplastic agents.

2. Drug Profile and Preformulation Studies:

- Collection of physicochemical data (solubility, pKa, stability, etc.).

3. Evaluation of Marketed Formulations

- Collection and analysis of marketed capecitabine tablets.
- Comparison based on:
- Hardness
- Friability
- Weight variation
- Disintegration time
- Drug content
- Dissolution profile

4. Comparative Therapeutic Assessment:

- Review and comparison of capecitabine's therapeutic potential with other antineoplastic agents.
- Discussion on efficacy, safety, and clinical relevance.
- Role in combination therapy and biomarker-based precision medicine.

DRUG PROFILE:

Description:

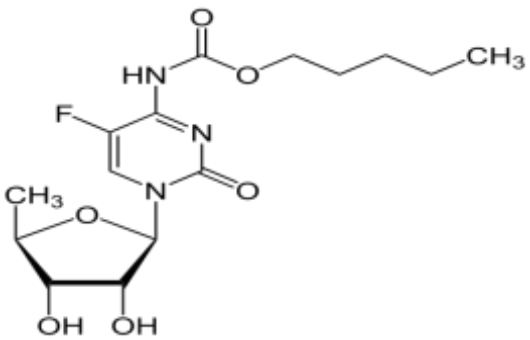
A chemotherapy medication used to treat various type of cancer which includes the gastric, breast and, colorectal cancers.

Generic Name: Capecitabine

Brand Name: *Ecansya, Xeloda*

Melting Point: The melting point of capecitabine is 123°C (decomposes). Some sources also indicate a range of 110-121°C.

Structure:



Chemical Formula: $C_{15}H_{22}FN_3O_6$
Chemical Name: pentyl *N*-[1-[(2*R*,3*R*,4*S*,5*R*)-3,4-dihydroxy-5-methyloxolan-2-yl]-5-fluoro-2-oxopyrimidin-4-yl] carbamate
Molecular Weight:
Average: 359.3501
Monoisotopic: 359.149263656
State of Drug: Solid.
Melting Point: 110-121 °C.
Solubility: Capecitabine has solubility in water. Solubility of capecitabine in water is 26 mg/ml.
Stability: Capecitabine tablets reportedly are stable for at least 9 months when stored in tightly closed containers at room temperature.
Mechanism of action: Capecitabine, fluoropyrimidine carbamate, is a prodrug of fluorouracil. It undergoes three-step enzymatic conversion to become cytotoxic. It is first metabolized in the liver to 5-deoxy-5-fluorocytidine (5-DFCR) by carboxylesterase, then to 5-deoxy-5-fluoroudine (5-DFUR) by cytidine deaminase, in both the liver and tumors. Conversion to active fluorouracil is mediated by thymidine phosphorylase, which is expressed in higher levels in tumors than in healthy tissues. Finally, capecitabine is catabolized to fluoro-beta-alanine by dihydropyrimidine dehydrogenase.
Absorption: The AUC of capecitabine and its metabolite 5'-DFCR increases proportionally over a dosage range of 500 mg/m2/day to 3,500 mg/m2/day (0.2 to 1.4 times the approved recommended dosage).
The AUC of capecitabine's metabolites 5'-DFUR and fluorouracil increased greater than proportional to the dose. The interpatient variability in the Cmax and AUC of fluorouracil was greater than 85%.
Following oral administration of capecitabine 1,255 mg/m^2 orally twice daily (the recommended dosage when used as a single agent), the median Tmax of capecitabine and its metabolite fluorouracil was approximately 1.5 hours and 2 hours, respectively.
Metabolism: Capecitabine undergoes metabolism by carboxylesterase and is hydrolyzed to 5'-DFCR. 5'-DFCR is subsequently converted to 5'-DFUR by cytidine deaminase. 5'-DFUR is then hydrolyzed by thymidine phosphorylase (dThdPase) enzymes to the active metabolite fluorouracil.
Fluorouracil is subsequently metabolized by dihydropyrimidine dehydrogenase to 5-fluoro-5, 6-dihydro-fluorouracil (FUH2).
The pyrimidine ring of FUH2 is cleaved by dihydropyrimidinase to yield 5-fluoro-ureido-propionic acid (FUPA). Finally, FUPA is cleaved by β-ureido-propionase to α-fluoro-β-alanine (FBAL).
Side Effects: Along with its needed effects, a medicine may cause some unwanted effects. Although not all of these side effects may occur.

More common

- 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
- Stomach pain
- Unusual tiredness or weakness

- Vomiting

Uses of capecitabine:

1. Stomach (Gastric) Cancer

In gastric cancer, Capecitabine is used in combination with cisplatin and/or epirubicin. It helps in managing advanced or inoperable gastric cancers and can improve survival when surgery is not an option or used as part of perioperative therapy (before and after surgery**).**

2. Breast Cancer

Capecitabine is commonly used to treat advanced or metastatic breast cancer, particularly in patients who have not responded to other chemotherapy drugs such as anthracyclines or taxanes. It can be used alone or in combination with other agents like docetaxel. It helps shrink tumors and control the spread of cancer**.**

3. Colorectal Cancer

Capecitabine is a standard treatment for colorectal cancer, including both colon and rectal cancer. It is used:

As adjuvant therapy after surgical removal of the tumor to prevent recurrence.

In metastatic colorectal cancer, where the cancer has spread to other parts of the body. It may be used alone or in combination with other drugs like oxaliplatin (in a regimen called CAPOX or XELOX).

4. Pancreatic Cancer

Capecitabine may be included in some chemotherapy regimens for pancreatic cancer, especially when used alongside radiotherapy (chemoradiation) or in combination with drugs like gemcitabine. It is typically used when other standard options are limited.

PREFORMULATION STUDIES OF CAPECITABINE :

Solubility of Capecitabine : Capecitabine is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide. The solubility of capecitabine in these solvents is approximately 5,12.5, and 14 mg/ml, respectively.

Capecitabine has a limited solubility in water Specifically ,it is soluble at 26mg/ml.

Solvent/Medium	Solubility(mg/ml)
Water	26mg/ml
Ethanol	5mg/ml
DMSO	12.5mg/ml
Dimethyl formamide	14mg/ml

Table No. 1: Solubility of Capecitabine

Evaluation Of Pre Compression Parameters Of The Powder Blend:

Pre compression parameters of the prepared powder blend of all the formulations were studied by determining the Bulk density, Tapped density, Compressibility Index, Hausner's ratio and Angle of repose.

Tablet code	Bulk Density(gm/cm^3)	Tapped Density(gm/cm^3)	Compressibility Index (%)	Hausner's Ratio(%)	Angle of Repose(º)
T1	0.382	0.535	26.31	1.35	31.31
T2	0.447	0.556	20.89	1.26	25.69
T3	0.382	0.552	22.38	1.28	38.63
T4	0.421	0.548	24.52	1.34	25.62
T5	0.412	0.568	26.62	1.28	25.62

Table No. 2: Result Of Pre Compression Parameters Of Capecitabine.

Evaluation of Post Compression Parameters of Capecitabine :

The compressed CPC tablets were subjected to various physical tests which include thickness, hardness, friability, weight variation, disintegration time and percentage drug content.

1. Thickness:

Tablet thickness was measured for 20 pre-weighed tablets from each batch using a digital Vernier scale. The average thickness was recorded in millimeters (mm).

The thickness should be controlled within a ±5% variation of the standard.

2. Weight Variation:

Ten tablets were randomly selected from each batch and weighed individually. The average weight was calculated.

According to USP specifications, the tablets meet the requirement if no more than 2 tablets deviate from the percentage limit, and no tablet exceeds twice the percentage limit.

3. Hardness Test:

The hardness or crushing strength, which is the force required to break a tablet in the radial direction, was measured using a hardness tester.

The hardness of 10 tablets was recorded, and the average hardness was calculated in kiloponds (KP).

4. Percentage Friability:

Friability testing evaluates the ability of tablets to resist abrasion and chipping during handling, transportation, and shipping. It provides an indication of mechanical strength.

Method:

If the weight of an individual tablet is greater than 655 mg, 10 tablets were taken and their initial total weight was recorded.

If the tablet weight is less than 655 mg, a number of tablets equivalent to a total weight of 6.55 g were used.

The tablets were placed in a Roche Friabilator and rotated for 100 revolutions at 25 rpm. After rotation, the tablets were dedusted and reweighed.

Calculation:

The percentage friability (% friability) is calculated as the percentage weight loss using the formula:

% Friability = (wo - wf) / wo x 100

Wo - initial weight of tablets, Wf - final weight of tablets

5. Percentage water content:

Karl Fischer reagent (sulphur dioxide and iodine dissolved in pyridine and methanol) is used to determine water content of the tablet using karl Fisher titrator.

Tablet Code	Thickness (mm)	Hardness (Kg/cm^3)	Weight Variation(mg)	Friability(%)	Disintegration Time(min.)	Percentage Drug Content
T1	5.66	7.5	658	0.89	10.47	98.1
T2	5.46	7.7	633	0.82	13.80	98.7
T3	5.58	8.4	650	0.88	14.01	99.0
T4	5.44	7.3	633	0.95	14.30	100.3
T5	5.72	7.4	655	0.79	13.98	98.9

Table No.3: Result of Post Compression Parameters Of Capecitabine.

6. Disintegration Time of Capecitabine:

Disintegration time refers to the duration required for a tablet to break up into smaller particles. The disintegration test is performed using an apparatus that includes a basket rack assembly containing six glass tubes, each measuring 7.75 cm in length and 2.15 mm in diameter, with a 10-mesh sieve at the bottom.

Fig.1: Disintegration Test of Capecitabine

The basket is raised and lowered 28 to 32 times per minute in 900 mL of medium maintained at 37°C. One tablet is placed in each tube, and the disintegration time is recorded as the time taken for the complete passage of tablet fragments through the 10-mesh sieve.

7.Dissoution Studies of Capecitabine:

Dissolution is the process by which a solid substance enters into a solution. In the pharmaceutical industry, it is defined as the amount of drug substance that dissolves in a solvent per unit time under standardized conditions of the liquid/solid interface, temperature, and solvent composition.

Dissolution is considered one of the most important quality control (QC) tests performed on pharmaceutical dosage forms. Moreover, it is now evolving into a valuable tool for predicting the bioavailability of drugs**.** Result of dissolution study are shown in Table.4 and Fig.1

A) Apparatus 1 (Basket Type):

In this method, a single tablet is placed in a wire mesh basket attached to the bottom of a shaft, which is connected to a variable speed motor. The basket is immersed in a dissolution medium contained in a 1000 mL cylindrical flask with a hemispherical bottom.

The medium is maintained at 37°C ± 0.5°C using a constant temperature bath. The motor is set to rotate at a specified speed, and samples of the fluid are withdrawn at regular intervals to determine the amount of drug dissolved in solution.

B) Apparatus 2 (Paddle Type):

This method is similar to Apparatus 1, except the basket is replaced with a paddle. The dosage form is allowed to sink to the bottom of the flask before stirring begins.

For dissolution testing, the USP specifies parameters such as the dissolution medium and its volume, the type of apparatus to be used, the RPM of the shaft, the time duration for the test, and the assay procedure. Test tolerance is expressed as a percentage of the labeled amount of drug that must be dissolved within the specified limit**.**

Fig.2: Dissolution Test of Capecitabine

Dissolution conditions:

Medium: water
Volume : 900ml
Temperature: 37oC ± 0.5oC
Apparatus: USP type –II (paddle)
RPM : 50
Time interval: 5, 10, 15, 20,30, up to 45 minutes.

Table No. 4: Dissolution Profiles of Capecitabine Innovator Product with Tablet 1 to Tablet 7.

Time(Mins.)	Drug Release(%)							
	Innovator	F1	F2	F4	F3	F5	F6	F7
5	28.2	38.4	39.7	26.5	29.5	24.5	32	17.7
10	55.2	70.1	74.2	56.28	59	46	66.2	49.2
20	74.1	87.2	91.8	75.6	84.6	63.8	88.8	58.7
30	88.1	91.3	98.2	87.8	93	76.9	92.2	91.2
45	98.7	97.5	101.3	99.89	100.1	95.2	99.3	97.7
60	100.6	97.8	103.9	100.8	101.8	105.1	102.3	101.7

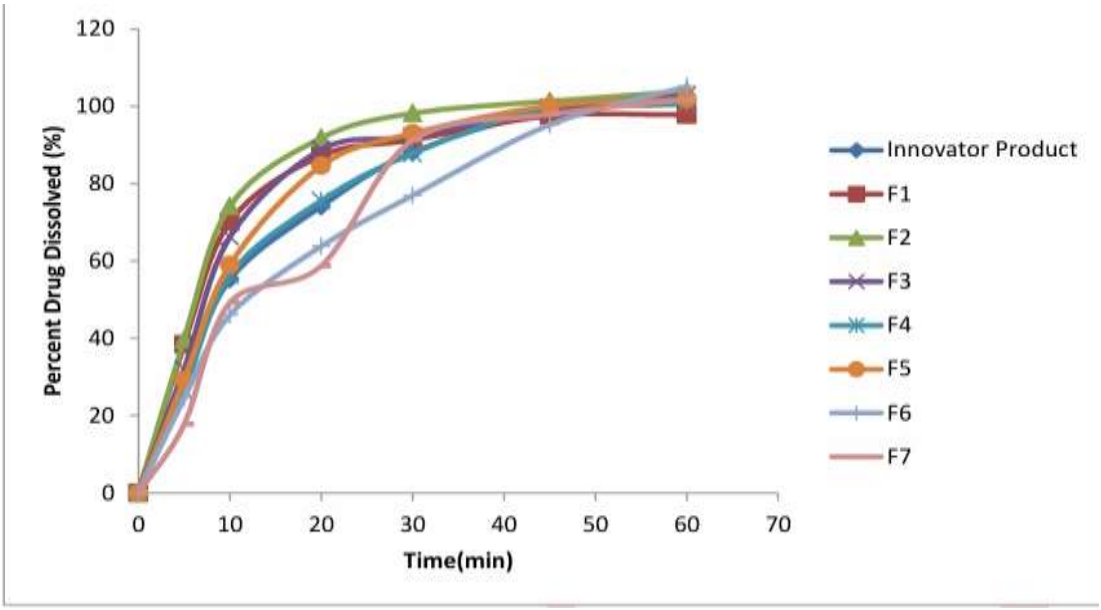


Fig.3: Dissolution Profiles of Capecitabine Innovator Product with F1 to F7 Formulations

RESULT & DISCUSSION:

The tablet blend were analysed for the parameters such as a bulk density, tapped density, compressibility index, Hausner's ratio, angle of repose, and the results were found within the limits. The solubility of capecitabine tablet was shown in the table No.1

The bulk density and tapped density values of formulations T1 to T5 range between 0.382–0.447 g/cc and 0.535–0.568 g/cc, respectively, as tabulated in Table 2. These values were found to be within acceptable limits.

The compressibility index, which is an indirect measure of bulk density, particle size, shape, surface area, and cohesiveness, ranged from 20.89% to 26.62% for T1 to T5 and is also presented in Table 2.

Hausner's ratio values for formulations T1 to T5 ranged between 1.26 and 1.35, as summarized in Table 4. The angle of repose, an indicator of flow properties, ranged from 25.62° to 38.63° for T1 to T5 and is reported in Table 2.

The hardness of each formulation (T1 to T5) was analyzed and found to be satisfactory, with values ranging from 10.4 to 13.8 kp. These results are presented in Table 3, and based on this, the formulations were selected for further studies. Tablet thickness was nearly uniform across all formulations, ranging from 5.44 to 5.72 mm, as shown in Table 3.

Although the total weight of each formulation was not maintained constant, the weight variation remained within the acceptable limit of 5%. These values are summarized in Table 3.

Friability values for all formulations were found to be less than 1%, indicating acceptable mechanical resistance, and are also reported in Table 3.

All tablets met the pharmacopoeial specifications for the disintegration of film-coated tablets, disintegrating within 15 minutes. The results are included in Table 3. Additionally, all formulations passed the assay test, with the percentage of active ingredient ranging from 98.1% to 100.3%.

In vitro dissolution studies of formulations F1 to F5 were conducted using water as the medium, and the percentage of drug release was calculated. All formulations were evaluated over a period of 45 minutes, and it was observed that each met the dissolution criteria of not less than (NLT) 90% drug release in 30 minutes.

The dissolution profiles of all formulations (F1–F5) were compared with that of the innovator product. Among them, formulation F4 exhibited a percentage of drug release closely matching that of the innovator, making it the optimized formulation.

The optimized blend (F4) was then compressed into tablets and evaluated for various parameters, including average weight, disintegration time, friability, thickness, and hardness. The in vitro dissolution profile of F4 confirmed its equivalence to the innovator product.

CONCLUSION:

The study successfully developed and evaluated capecitabine tablet formulations (F1–F5), focusing on pre-compression and post-compression parameters to ensure quality and performance. All formulations demonstrated acceptable flow properties (bulk density, tapped density, compressibility index, Hausner's ratio, and angle of repose), as well as satisfactory mechanical characteristics (hardness, friability, thickness, and weight variation).

Disintegration times were within pharmacopoeial limits, and all formulations passed the assay test with acceptable drug content.

In vitro dissolution studies confirmed that all formulations released more than 90% of the drug within 30 minutes, meeting the required specifications. Among them, formulation F4 exhibited a dissolution profile most closely matching the innovator product, indicating its potential as an optimized and bioequivalent alternative.

Therefore, formulation F4 can be concluded as the optimized capecitabine tablet formulation based on its superior dissolution characteristics and compliance with all quality parameters.

THERAPEUTIC ASSESSMENT OF CAPECITABINE :

Capecitabine is often chosen as a first-line therapy for gastric cancer and breast cancer because it provides a favorable balance of efficacy, convenience, and tolerability, especially when used as part of a combination regimen.

Capecitabine is a key anticancer drug widely used for the treatment of gastric, breast and colorectal cancers. Its frequent prescription necessitates appropriate follow-up and post-prescription monitoring to ensure proper treatment administration and manage potential adverse effects.

Objective:

The objective of this study was to assess the level of knowledge among patients regarding their treatment with capecitabine at the day hospital of an oncology facility.

Methodology:

This prospective study was conducted over a two-month period (February to April 2025) at the Day Hospital in the Government Hospital of Cancer, Chatrapati Sambhajinagar.

Data were collected using a structured questionnaire to evaluate patients' understanding of their capecitabine therapy.

Results:

A total of 45 patients participated in the study. Among them, 76% reported having received pharmaceutical advice about capecitabine treatment. The primary indications for therapy were gastric and breast cancers. Notably, 97% of the patients were aware of the indication for capecitabine and its therapeutic action on their specific tumor type. Furthermore, 23% of patients reported experiencing side effects, with hand-foot syndrome being the most frequently reported, accounting for 3% of all side effects.

Capecitabine remains an oral treatment of choice for both gastric and breast cancer. Therapeutic education plays a crucial role in optimizing treatment outcomes and managing side effects, thereby improving patient adherence and quality of life. Capecitabine is an oral fluoropyrimidine approved by the FDA for use as a first-line therapy in patients with metastatic breast, gastric and colorectal cancer when single-agent fluoropyrimidine therapy is preferred.

Some question asked to the physician about the Capecitabine therapeutic assessment and their perspective about the Capecitabine noted which is listed below:

1. In which patients the Capecitabine is used ?

Capecitabine tablets are primarily used in adult patients with certain types of solid tumors, particularly in:

Breast Cancer :

Metastatic breast cancer: Capecitabine is commonly used when patients have progressed after treatment with anthracyclines (like doxorubicin) and taxanes (like paclitaxel).

It may also be used in combination therapy with docetaxel or as a maintenance/adjuvant therapy in some cases.

Gastric Cancer:

Capecitabine is used in advanced or metastatic gastric cancer, often in combination with platinum-based agents like oxaliplatin or cisplatin (e.g., in the XELOX regimen).

It is a good alternative to intravenous 5-FU, offering similar efficacy with the convenience of oral administration.

2. What are the symptoms of gastric and breast cancer ?

The symptoms of gastric (stomach) and breast cancer can vary depending on the stage of the disease, but here are the most common signs:

Gastric Cancer (Stomach Cancer) :Common Symptoms:

a. Persistent indigestion or heartburn
b. Loss of appetite
c. Unexplained weight loss
d. Nausea or vomiting (sometimes with blood)
e. Feeling full after eating small amounts
f. Stomach pain or discomfort, especially in the upper abdomen
g. Fatigue or weakness
h. Black or tarry stools (due to bleeding)

Note: Early-stage gastric cancer often causes no symptoms or very mild digestive issues, which can delay diagnosis.

Breast Cancer :Common Symptoms:

a. A lump or thickening in the breast or underarm area
b. Change in size or shape of the breast
c. Dimpling or puckering of the skin
d. Nipple discharge (especially if bloody)
e. Nipple inversion or pain
f. Redness or scaling of the nipple or breast skin
g. Swelling in part or all of the breast

3. From both the medicine Capecitabine or Doxorubicin which one has best result in gastric and beast cancer and why ?

The choice between Capecitabine and Doxorubicin depends on the type of cancer, stage, patient profile, and treatment goals.

Both drugs are effective, but they have different roles in treatment. Here's a comparative assessment:

1. Breast Cancer:

Doxorubicin is a core drug in the treatment of early-stage and metastatic breast cancer, especially in combination regimens like AC (Adriamycin [Doxorubicin] + Cyclophosphamide). It has a high response rate and is often used as part of first-line therapy.

Capecitabine is usually used in metastatic or recurrent breast cancer, particularly in patients who have previously received anthracyclines (like doxorubicin) and taxanes. It is also used as maintenance or for HER2-negative disease in some cases.

Clinical Perspective:

Doxorubicin is often more effective early in treatment, but its use is limited by cardiotoxicity.

Capecitabine offers good efficacy with better tolerability and is especially beneficial for long-term oral therapy in metastatic disease.

2. Gastric Cancer:

Doxorubicin is not commonly used in modern gastric cancer treatment due to limited efficacy and high toxicity. It was included in older regimens (like ECF), but has largely been replaced by more effective and tolerable combinations.

Capecitabine, on the other hand, is widely used as a first-line agent in advanced or metastatic gastric cancer. It is often combined with oxaliplatin or cisplatin (e.g., XELOX regimen) and has shown outcomes comparable or superior to 5-FU-based regimens.

Clinical Perspective:

In gastric cancer, Capecitabine is clearly preferred over Doxorubicin due to better efficacy, fewer side effects, and oral administration.

Why Capecitabine often has the advantage:

a. Oral administration
b. Fewer long-term toxicities (especially no cardiotoxicity)
c. Proven effectiveness, especially in gastric cancer
d. Better patient compliance and quality of life

So, while Doxorubicin is critical in early breast cancer, Capecitabine offers more flexibility, safety, and broader use, especially in gastric and metastatic breast cancer.

4. Why this tablet is useful in gastric and breast cancer ?

Capecitabine is useful in both gastric and breast cancer because of its targeted mechanism, proven clinical efficacy, and favorable administration route. Here’s why it plays a key role in treating these cancers:

1. Targeted Mechanism of Action:

Capecitabine is an oral prodrug of 5-fluorouracil (5-FU).

It is selectively activated within tumor cells by the enzyme thymidine phosphorylase, which is found in higher concentrations in cancer tissues. This allows for more localized activity, minimizing systemic toxicity and enhancing its anti-cancer effect.

2. In Gastric Cancer:

Capecitabine is widely used in advanced or metastatic gastric cancer, especially in combination with platinum agents like oxaliplatin (e.g., XELOX regimen).It has shown non-inferior or superior efficacy compared to continuous 5-FU infusion, with added convenience of oral administration.

It helps in shrinking tumors, delaying progression, and improving survival in both first-line and adjuvant settings.

3. In Breast Cancer:

Capecitabine is used primarily in metastatic breast cancer, especially when patients have failed anthracycline- and taxane-based regimens.

It offers a well-tolerated oral alternative, making it ideal for long-term treatment and maintenance.

It is also effective in HER2-negative breast cancer, and may be used in combination with other agents like docetaxel.

4. Additional Advantages:

a. Oral route of administration improves patient convenience and quality of life.
b. Lower risk of cardiotoxicity compared to anthracyclines like doxorubicin.
c. Manageable side effect profile, especially when monitored properly (e.g., hand-foot syndrome, GI effects).

Some question asked to the patients who are suffering from the cancer what is their experience with Capecitabine tablet treatment therapeutic and their perspective about the Capecitabine is noted which is listed below:

1. What is your result experience when taking the capecitabine tablet as a medicine?

My experience with Capecitabine tablets has been a mix of positive results and some manageable side effects.

I was prescribed it as part of my treatment for breast/gastric cancer, and I appreciated that it's an oral medication—being able to take it at home made things a bit easier emotionally and physically. In terms of results, I noticed a gradual improvement based on my scans and blood work. My doctor said the tumor had shrunk, and some symptoms I was experiencing became less intense. That gave me hope.

As for side effects, I did have some issues—mainly fatigue, nausea, and hand-foot syndrome. My hands and feet became red and sore after a few weeks, but I was given creams and advice that helped. Diarrhea and loss of appetite were also present, but not severe for me.Overall, I feel that Capecitabine has helped me make progress in my cancer treatment with fewer hospital visits and more time at home. It's not always easy, but it's been effective and tolerable for me.

2. From how many days you are taking the medicine ?

I've been taking Capecitabine for about 3 months now, following the cycle my doctor prescribed—usually 14 days on the medicine and then 7 days off to let my body recover. Each cycle feels a bit different, but over time, I've learned how to manage the side effects better.

During the first few weeks, my body was still adjusting. By the second cycle, I started noticing changes in my energy levels and some improvements in my condition, according to my test results. Now, after 3 months, it has become a routine, and I feel more confident in handling the treatment.

3. In how many days you had got a relief from disease ?

I started noticing some relief after about 4 to 6 weeks of taking Capecitabine. The symptoms that were bothering me the most like pain, fatigue, and loss of appetite began to ease gradually. I didn't feel

completely better right away, but my scans after two cycles showed that the treatment was working, and the tumor was shrinking.

It's important to understand that with cancer treatment, "relief" doesn't always mean being cured right away, but rather feeling improvement and gaining better control over the disease. For me, that early progress gave me hope and the strength to continue with the medication.

4. According to you which is best medicine for gastric/breast cancer Capecitabine or Doxorubicin or Trifluridine ?

From my experience, I believe Capecitabine has been the best option for me compared to Doxorubicin or Trifluridine. I've been on Capecitabine for a few months now, and it has helped control my cancer with manageable side effects. The fact that I can take it at home, as a tablet, makes a big difference less hospital time and more comfort.

I was told that Doxorubicin works well too, especially in breast cancer, but it can cause serious heart problems if used too long. That made me nervous, and my doctor also felt Capecitabine was a safer choice for my situation .As for Trifluridine, I heard it's used more when other treatments stop working, especially for gastric cancer. I haven't used it personally, but I know it's usually a later option.

So for me, Capecitabine has been effective, easier to manage, and more suitable for long-term treatment. But every patient is different, and what works best really depends on the stage of the cancer, overall health, and how the body reacts to each drug.

Here's a detailed explanation from a physician's perspective why they choose a Capecitabine first line treatment for gastric and colon cancer :

1. Comparable or Superior Efficacy to 5-FU

Capecitabine is an oral prodrug of 5-fluorouracil (5-FU), and numerous clinical trials have demonstrated that:

It is non-inferior or slightly superior to continuous infusion 5-FU in terms of response rate and overall survival.

Trials like the REAL-2 and ML17032 studies showed Capecitabine-containing regimens (e.g., XELOX) perform at least as well as 5-FU-based regimens (e.g., FOLFOX or ECF).

Thus, Capecitabine can safely and effectively replace 5-FU in many standard protocols.

2. Oral Administration Improves Patient Quality of Life

a. Capecitabine is administered orally, which provides multiple practical and clinical advantages:
b. Eliminates need for central venous access.
c. Reduces hospital visits, especially beneficial in elderly or palliative patients.
d. Increases patient comfort and autonomy during treatment.
e. This is particularly important in outpatient settings and during long-term treatment.

3. Synergistic Potential in Combination Regimens

Capecitabine is highly effective when combined with other chemotherapeutic agents:

XELOX (Capecitabine + Oxaliplatin) is a well-established first-line regimen in advanced gastric cancer.

Works well with cisplatin, irinotecan, and trastuzumab (for HER2-positive tumors).

Offers flexibility in designing regimens for both curative and palliative intent.

4. Resource and Cost Considerations

Capecitabine is more cost-effective than IV 5-FU when considering hospitalization, infusion pump costs, and catheter care. Reduced clinic time translates to better resource utilization in busy oncology settings.

7. Global Guidelines Support Its Use

NCCN, ESMO, and ASCO guidelines list Capecitabine as an acceptable alternative to 5-FU in first-line therapy for advanced or metastatic gastric and gastroesophageal cancers.

Regimens like XELOX and XP (Capecitabine + Cisplatin) are commonly recommended.

COMPARATIVE STUDY OF CAPECITABINE WITH OTHER DRUGS:

Efficacy (Clinical Outcomes): The efficacy (clinical outcomes) of Capecitabine is compared with other antineoplastic agent in the breast and gastric cancer which is listed below:

Breast Cancer:

- Capecitabine shows non-inferior survival compared to IV 5-FU regimens; useful in adjuvant and metastatic settings.
- Doxorubicin is very effective but limited by cumulative dose cardiotoxicity.
- Trifluridine lacks sufficient data in breast cancer; not standard.

Gastric Cancer:

- Capecitabine + oxaliplatin (XELOX) has shown similar or better efficacy than 5-FU/leucovorin regimens.
- Doxorubicin is less favored due to toxicity and limited incremental benefit.
- Trifluridine/tipiracil (TAS-102) shows modest survival benefit in heavily pretreated cases.

Indications & Tumor Specificity:

Drug	Breast Cancer	Gastric Cancer
Capecitabine	Widely used; often in combination (e.g., with docetaxel)	Used in advanced/metastatic cases, especially HER2-negative
Doxorubicin	Key drug in breast cancer (esp. triple-negative); limited use due to cardiotoxicity	Limited efficacy; not first-line in gastric cancer
Trifluridine	Not typically used	Used in refractory gastric cancer as FTD/TPI (TAS-102)

Table No. 5: Comparative study of indications & tumor specificity of Capecitabine, Doxorubicin and Trifluridine in breast and gastric cancer.

Mechanism Of Action:

Drug	Mechanism Of Action
Capecitabine	Oral prodrug converted to 5-FU in tumor cells; inhibits thymidylate synthase → inhibits DNA synthesis.
Doxorubicin	Anthracycline antibiotic; intercalates DNA and inhibits topoisomerase II; generates free radicals.
Trifluridine	Incorporated into DNA, causing DNA dysfunction; combined with tipiracil to prevent degradation.

Table No.6: Comparative mechanism of action of Capecitabine, Doxorubicin and Trifluridine .

Administration & Patient Compliance:

- Capecitabine: Oral; highly preferred by patients, improves QOL.
- Doxorubicin: IV; requires hospital visits, infusion reactions possible.
- Trifluridine: Oral; requires strict schedule, usually salvage therapy.

Toxicity Profile:

Drug	Common Toxicities	Notable Issues
Capecitabine	Hand-foot syndrome, diarrhea, mucositis	Safer profile; oral
Doxorubicin	Myelosuppression, nausea	Cumulative cardiotoxicity, alopecia
Trifluridine	Neutropenia, anemia, fatigue	Mostly hematologic toxicity

Table No.7: Toxicity profiles of Capecitabine, Doxorubicin and Trifluridine.

Drug Resistance:

- Capecitabine: Resistance via thymidylate synthase upregulation or DPD overexpression.
- Doxorubicin: Resistance via P-glycoprotein efflux and DNA repair.
- Trifluridine: Resistance through decreased incorporation or thymidine kinase downregulation.

Conclusion:

Capecitabine offers a more favorable balance of efficacy, tolerability, and convenience compared to doxorubicin and trifluridine in breast and gastric cancers, particularly:

- In breast cancer, it is a strong alternative or adjunct to anthracyclines, especially in older or cardiac-risk patients.
- In gastric cancer, it is first-line in combination regimens, while trifluridine is reserved for salvage therapy and doxorubicin is rarely used due to poor risk-benefit ratio.

REFERENCES

1. Walko CM, Lindley C: Capecitabine: a review. Clin Ther. 2005 Jan;27(1):23-44.
2. Wagstaff AJ, Ibbotson T, Goa KL: Capecitabine: a review of its pharmacology and therapeutic efficacy in the management of advanced breast cancer. Drugs. 2003;63(2):217-36.
3. Koukourakis GV, Kouloulias V, Koukourakis MJ, Zacharias GA, Zabatis H, Kouvaris J: Efficacy of the oral fluorouracil pro-drug capecitabine in cancer treatment: a review. Molecules. 2008 Aug 27;13(8):1897-922.
4. Twelves C: Vision of the future: capecitabine. Oncologist. 2001;6 Suppl 4:35-9
5. Vasey PA, McMahon L, Paul J, Reed N, Kaye SB: A phase II trial of capecitabine (Xeloda) in recurrent ovarian cancer. Br J Cancer. 2003 Nov 17;89(10):1843-8. doi: 10.1038/sj.bjc.6601381.
6. Alqahtani S, Alzaidi R, Alsultan A, Asiri A, Asiri Y, Alsaleh K: Clinical pharmacokinetics of capecitabine and its metabolites in colorectal cancer patients. Saudi Pharm J. 2022 May;30(5):527-531.
7. Milano G, Ferrero JM, Francois E: Comparative pharmacology of oral fluoropyrimidines: a focus on pharmacokinetics, pharmacodynamics and pharmacomodulation. Br J Cancer. 2004 Aug 16;91(4):613-7.

8. Strosberg JR, Fine RL, Choi J, Nasir A, Coppola D, Chen DT, Helm J, Kvols L: First-line chemotherapy with capecitabine and temozolomide in patients with metastatic pancreatic endocrine carcinomas. Cancer. 2011 Jan 15;117(2):268-75
9. Fine RL, Gulati AP, Krantz BA, Moss RA, Schreibman S, Tsushima DA, Mowatt KB, Dinnen RD, Mao Y, Stevens PD, Schrope B, Allendorf J, Lee JA, Sherman WH, Chabot JA: Capecitabine and temozolomide (CAPTEM) for metastatic, well-differentiated neuroendocrine cancers: The Pancreas Center at Columbia University experience. Cancer Chemother Pharmacol. 2013 Mar;71(3):663-70.
10. Wolf JK, Bodurka DC, Verschraegen C, Sun CC, Branham D, Jenkins AD, Atkinson N, Gershenson DM: A phase II trial of oral capecitabine in patients with platinum--and taxane--refractory ovarian, fallopian tube, or peritoneal cancer. Gynecol Oncol. 2006 Sep;102(3):468-74.
11. Chaudhari PD. Formulation and evaluation of fast dissolving tablets of famotidine. Indian Drugs. 2005: 42(10); 641-649.
12. Dinesh Bhandari. Recent Trends Fast dissolving tablets. www.Pharminfo.net
13. Jantratid E. Reported the biowavier Monographs for immediately release solid dosage forms cimetidine. Journal of Pharmaceutical Sciences.2006: 95; 974–984
14. Meyer. The bioequivalence of methylphenidate Immediate Release tablets, Journal of Pharmaceutical research. 2000:17; 381-384.
15. Nansri Saha Ghosh et.al. Formulation of immediate release dosage form of Ranitidine HCl tablets using HPMC and starch acetate film former. J. Chem. Pharm. Res. 2010: 2(3);147-157.
16. Pani et.al. Formulation, development and optimization of immediate release tablets by factorial design .Drug discoveries and therapeutics.2009: 4(6); 453-458.
17. Rawlings E A.2003.Bently text book of pharmaceutics, 8th edition: pp.269.
18. Remington J. Remington: The Science and Practice of Pharmacy; Nineteenth Edition, 2: 1615-1641.