# Dhaka University Nanotechnology Centre (DUNC)
# University of Dhaka
# Dhaka 1000, Bangladesh
# Project Proposal for 2025-26

**Inception Report:**

1. **Title of the Proposed Research Project: Development and Characterization of Stomach Targeted Floating Alginate NanoBeads of Anticancer drug 5-Flurouracil Using QbD Approach for Gastric Cancer**

**2. Name of the Project Investigators with affiliation:**

**i) Principal Investigator**

Dr. Jakir Ahmed Chowdhury
Professor and chairman, Department of Pharmacy, Faculty of Pharmacy, University of Dhaka

**ii) Co- Investigator**

Dr. Md. Raihan Sarkar
Associate Professor, Department of Pharmaceutical Technology, Faculty of Pharmacy, University of Dhaka

**3. Place where the work will be performed:** The research work for this project will be conducted in the Dept. of pharmaceutical Technology Laboratory and Faculty of Pharmacy Laboratory at University of Dhaka.

**4. Outline of the project with background information:**

**4.1 Introduction**

Globally, gastric cancer is one of the primary causes of cancer-related deaths. It develops when cells lining the digestive tract acquire mutations that cause uncontrolled growth (1). Main risk factors include a history of chronic Helicobacter pylori infection, smoking, excessive alcohol consumption, obesity, infections like Epstein-Barr virus, a person's genetic makeup, and advanced age. More than 1,089,000 people were diagnosed with stomach cancer in 2020, and around 769,000 people lost their lives to this disease (2).

**4.1.1 Treatment option for stomach cancer**

**(I) Chemotherapy**

Chemotherapy uses drugs that fight cancer, like cisplatin, or docetaxel, to kill cancer cells that are growing quickly. It is effective at inhibiting cancer from growing, but it has some big problems. These include non-specific toxicity that harms healthy cells, a short plasma half-life for drugs like 5-FU, and serious adverse effects like vomiting, hair loss, nausea, and bone marrow suppression.

**(II) Surgery**

Surgery refers to eliminating out part of the stomach and nearby lymph nodes. It is best for stomach cancer that is still in its early stages. But there are some drawbacks such as the chance of infection, bleeding, and problems with nutrition after surgery. In addition, surgery doesn't work for cancer that has spread or is in an advanced stage.

**(III) Radiation therapy**

In this treatment high-energy rays are used to destroy cancer cells. Normally these are combinedly used with chemotherapy. Radiation therapy shrink tumours cell but it can also damage some nearest healthy cell, which can cause side effects such as loss of fatigue, appetite, vomiting nausea etc.

**(IV) Immunotherapy**

Immunotherapy helps the immune system find and kill cancer cells. Some kinds of stomach cancer can be treated with drugs like pembrolizumab. This treatment works only for people with certain biomarkers, and it can also cause problems with the immune system (3-4).

**(V) Targeted therapy**

Target therapies are used to kill cancer cells by using molecular targets. For example, HER2-positive gastric cancer is one type of cancer that are treated by targeted therapy. The major drawback of this therapy is that it only effective for some types of cancer and is very expensive. Cancer cells can also become resistant to targeted drugs over time.

There are some limitations to all of the current treatments for stomach cancer. Surgery is invasive and only effective in the early stages. Chemotherapy has a short half-life and can cause serious side effects throughout the body. Radiation therapy can hurt healthy tissues nearby, and targeted therapy and immunotherapy are costly and only work for some patients. Because of these problems, a more effective drug delivery system will be needed.5-Fluorouracil floating beads will be selected to overcome these limitations because cconventional chemotherapy of 5-flurouracil is often limited by poor absorption, rapid gastric emptying and systemic side effect(5)
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### 4.1.2 Floating beads

Floating drug delivery system has emerged as a promising strategy to prolong gastric residence time. The retention of a drug delivery system in the stomach extends the overall gastrointestinal transit time. Floating nano beads are less dense, so they can float on stomach fluids and stay in the stomach for 8 to 12 hours, while the normal time for the stomach to empty is only 3 to 4 hours. This prolonged gastric retention allows for controlled and sustained drug release, higher absorption bioavailability, and lower systemic toxicity (6).

### 4.1.3 Alginate nano and micro beads

Alginate, a biocompatible and biodegradable polymer, can form Nano beads through emulsion techniques, providing a nano-scale carrier for controlled drug release. Alginate beads are nano

scale carriers that encapsulated the drug in alginate polymer matrix(8).Combining alginate nano beads with floating system offers an effective strategy for stomach targeted chemotherapy.

### 4.1.4 Study Design

The process can be divided into three main stages: preparation of alginate nano beads formulations, optimization by DoE, and characterization of optimized formulations (morphological and compatibility studies).

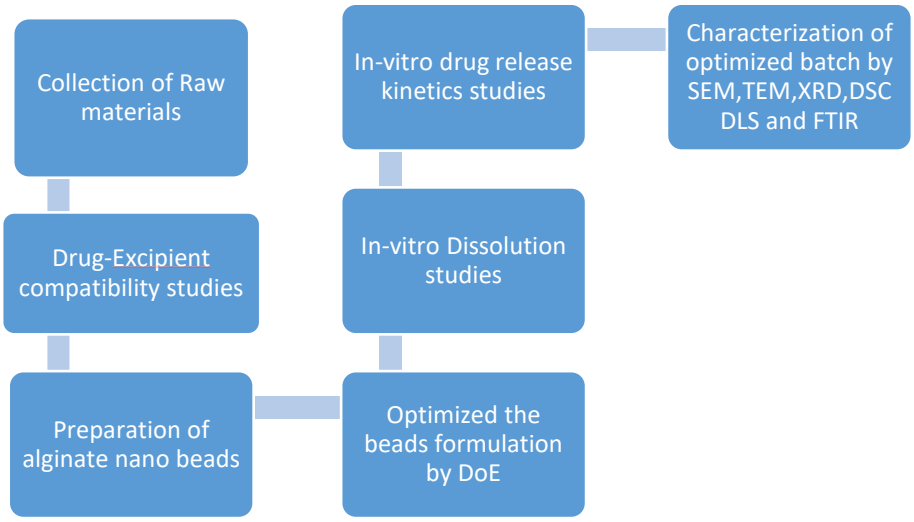


**Figure: Schematic diagram of study design of beads preparation**

## 4.2 Methodology

### 4.2.1 Preparationof alginate 5-fluorouracil beads

Sodium alginate solutions of various concentrations will be manufactured by dissolving the essential amount of alginate in water with gentle stirring using a magnetic stirrer. After 5-fluorouracil will be added into an alginate solution with continuous stirring to ensure uniform mixture. Subsequently, paraffin oil will be gradually added into the dispersion while maintaining continuous agitation to ensure homogeneous mixing. Sonication will be applied for 30 minutes to eliminate any air bubbles from dispersion. The resultant dispersion will injected by a 22-gauge syringe needle into 4% (w/v) calcium chloride solution at room temperature under continuous stirring by high shear mixture. The produced beads will be allowed to remain in the calcium chloride solution for 5 minutes. The beads will be collected by evaporating the water (8,9).

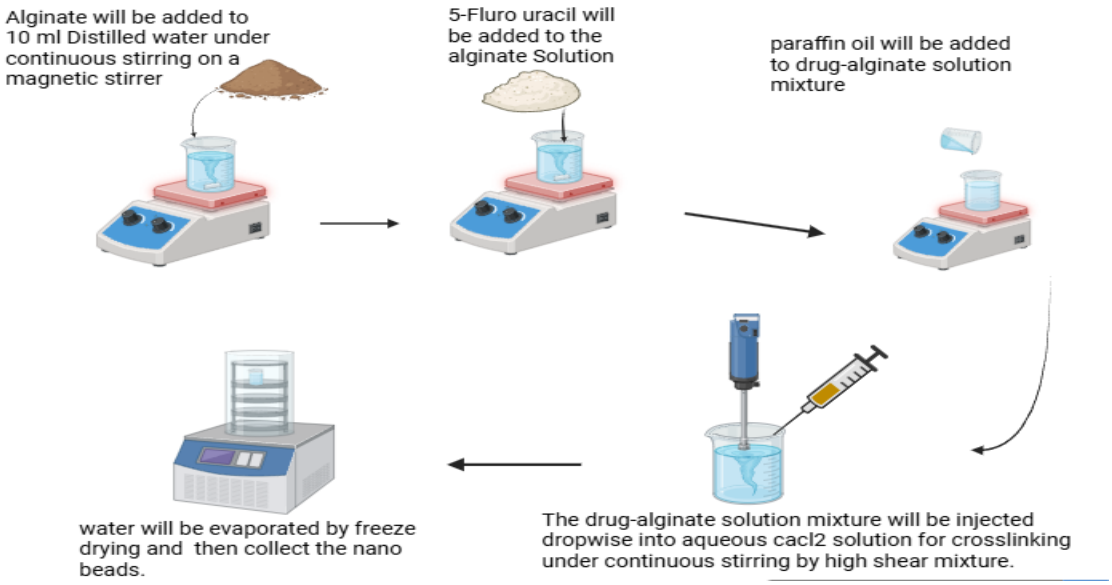


**Figure: Preparation process of 5-fluorouracil beads**

### 4.2.2 Optimizations of beads formulation by DoE

A central composite experimental design will be applying response surface methods to carry out assessing the relationship among independent variables, their responses, and their interactions inside an effective model. The model is a $3^2$ full factorial design. The experimental design included two variables and four responses. The calculated dependent response factor variables were percentage of floating, particle cumulative drug release, and entrapment efficiency (10).

### 4.2.3 Characterization of Optimized Alginate 5-fluorouracil Nanobeads

The optimized alginate beads will be characterized using the following techniques:

- X-ray Diffraction (XRD): To detect the crystalline or amorphous nature of the beads and any structural changes due to crosslinking or incorporation of additives.
- Fourier Transform Infrared Spectroscopy (FTIR): To determine functional groups and find out chemical interactions and stability of formulation between drug and excipients.
- Dynamic Light Scattering (DLS): DLS will determine particle size distribution and polydispersity index (PDI) and zeta potential that will assess surface charge.
- Scanning Electron Microscopy (SEM): To observe surface morphology, shape, and porosity of the beads.
- Transmission Electron Microscopy (TEM): For high-resolution imaging to visualize internal structure and Nano scale particle size.
- Differential Scanning Calorimetry (DSC): To study melting point, glass transition, and stability of the drug, polymer and polymer matrix.

- **4.3 Objectives of the study**

  The aims of this research work are:

- Design and formulate 5-fluorouracil encapsulated floating alginate beads
- Enhance floating time, extend stomach retention, and maintain drug release.
- Try to reduce the size of the beads in nano-level
- Optimized the alginate beads formulation by DoE
- Characterization and Evaluation of the optimized formulated beads

**4.4 Expected Outcome**

The expected outcomes of the project:

- Boost the absorption of 5-fluorouracil and improve its bioavailability in the stomach
- Enhance the 5-fluorouracil local therapeutic efficacy against gastric cancer.
- Slow and sustain release of 5-FU
- Reduce systemic toxicity, particularly gastrointestinal and hematological adverse effects.
- Increase patient satisfaction by reducing dose frequency.

**5. Rational of the project and its importance**

Cancer in stomach is one of the most challenging cancers for treatment due to less gastric emptying time that causes inadequate drug absorption hence low therapeutic activity.The chemo therapy of stomach cancer also causes systemic adverse effects.Traditional treatments such as surgery, chemotherapy, and radiotherapy doesn't often accomplish ideal therapeutic results that emphasize the requisite for more accurate and effective drug delivery methods.The application of floating alginate beads for targeted therapy in stomach cancer remains predominantly unaddressed.Gastro-retentive nano-technologies, including floating beads, exhibit potential in extending gastric residence time, regulated release and enabling drug absorption. Alginate-based formulations exhibit biocompatibility, produce stable gels, and are suitable for stomach environments, rendering them ideal for targeted drug delivery.

The importance of this work includes:

- Extended gastric retention: Floating beads of 5-FU may remain in the stomach for aprolongedperiod, enablingextended and localized release of this API.

- Targeted therapy: Concentrating on gastric cancer cells diminishes systemic side effects relative to traditional chemotherapy.
- Boosted bioavailability: Nano sizing improves 5-FU solubility and absorption through stomach tissues.

- Novelty: The combination of floating, gastro-retentive, and nano sized alginate beads for the treatment of stomach cancer is predominantly unexamined in the current literature.

The aim of this study is to improve therapeutic efficacy of 5-Fluro uracil for gastric cancer by retaining the formulation in stomach for longer period of time. Floating alginate beads will enhance local concentration of 5-fluro uracil. Due to size,the alginate beads will enhance drug permeability.This system also will minimize systemic toxicity. Incorporating the QbD approach will ensures a robust, reproducible and regulatory compliant formulation.This study is significant due to its combination of nano-technology and floating drug delivery system to produce a safer, targeted and effective oral chemotherapy.

**6. Previous Experience of the Project Supervisor(s) in the area of Nanotechnology:**

Both Principal and co-investigator work on design of drug formulations such as solid dispersion, immediate release formulations; sustain release formulation, microsphere formulations

**7. Time required for completion of the project:** 1-12-2025 to 30-6-2026

| Project major Activities | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| Literature review, **Already done** | | | | | | |
| Protocol design , **Already done** And collection of materials | | | | | | |
| Formulation development | | | | | | |
| In-vitro characterization of formulation | | | | | | |
| Stability studies of formulation | | | | | | |
| Data analysis and report writing | | | | | | |

**8. Current status of the project work**

A comprehensive literature review has been carried out to formulate the dosage form. The study protocol has been developed. A number of preliminary Trial formulations have been developed and currently exploration is going on. After getting the allocated fund, different API and reagents will be purchased and lab work will begin.

Preliminary formulations composition for 5-Fluro Uracil loaded nano alginate beads.

| n code | (mg) | Alginate Concentration | Paraffin Oil %(w/v) | chloride %(w/v) | HPMC 100Mcps | Time (minute) |
|---|---|---|---|---|---|---|
| F(blank) | 100 | 3 | 0 | 4 | 9:1 | 5 |
| F1 | 100 | 3 | 10 | 4 | 9:1 | 5 |
| F2 | 100 | 4 | 10 | 3 | 9:1 | 5 |
| F3 | 100 | 2 | 10 | 2 | 9:1 | 5 |

**9. Fund**

**Research Fellowship: 12000*3= 36000/=**

Name:-Md Hafez Ahmed

Departement:- Pharmaceutical Technology, Dhaka university

Class:-M.pharm Student

Session:-2022-23

**(b) Apparatus, API, Polymer, Chemicals and Analytical Services: 27,000/=**

DoE apps subscription, Pipette, filter paper, syringe, 5- Fluro uracil, Alginate, paraffin Oil, solvents, and other polymers will be purchased. XRD, SEM, DLS, SEM, TEM, and DSC will be used to characterize the formulations.

## Total fund allocated: 63,000/=

**10. Any financial assistance received/to be received from any other source for this project: no**

**11. References**


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Thanks
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