

Design and Evaluation of Microsponge Infused with Naturally Derived Anticancer Agent

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Abstract: *The present study focuses on the design and evaluation of a microsponge-based drug delivery system infused with a naturally derived anticancer agent. Natural compounds have gained significant attention in cancer therapy due to their biocompatibility and reduced side effects; however, their clinical application is often limited by poor solubility and stability. To overcome these challenges, a microsponge delivery system was developed to enhance controlled release and therapeutic efficiency of the selected natural anticancer agent.*

Keywords: Microsponge drug delivery system; Naturally derived anticancer agent; Controlled drug release; Drug encapsulation; Polymer-based delivery; Sustained release; Cancer therapy; Biocompatibility

I. INTRODUCTION

1. CANCER

Cancer is a diverse group of diseases that arise from the uncontrolled proliferation of cells. These malignant cells can invade surrounding tissues and spread to other parts of the body, a process known as metastasis. The World Health Organization (WHO) reported that cancer caused approximately 10 million deaths in 2020, making it the second leading cause of death globally.^[1]

1.1 HERBAL ANTICANCER AGENT

Herbal anticancer agents are natural compounds derived from plants that have demonstrated potential in inhibiting the growth and spread of cancer cells. Unlike conventional chemotherapy, which non-selectively targets all rapidly dividing cells and often results in severe side effects, many herbal agents are believed to act more selectively, targeting cancer cells while sparing normal tissues.^[2]

1.2 ANTICANCER AGENT

An anticancer drug is any medication effective in treating malignant or cancerous diseases. These drugs fall into several major classes: alkylating agents, antimetabolites, natural products, and hormones.

Alkylating agents and related compounds, which form covalent bonds with DNA to impede its replication.

Antimetabolites, which disrupt essential metabolic pathways involved in DNA synthesis.

Cytotoxic antibiotics, originating from microbial sources, that prevent mammalian cell division.

Plant derivatives, such as vinca alkaloids, taxanes, and camptothecins, which target microtubule function and interfere with the mitotic spindle formation.^[3]



CLASIFICATION OF ANTICANCER AGENT

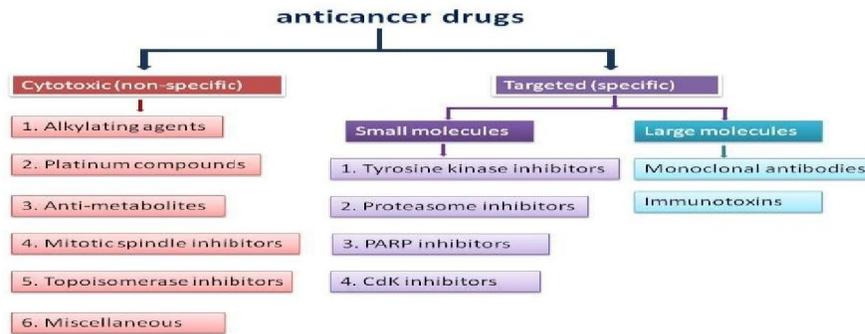


Fig.no. 1: Classification of anticancer agents [4]

1.3 MECHANISM ACTION ANTICANCER AGENT

Anticancer agents, also known as chemotherapeutic drugs, are medications used to destroy, kill, shrink, or slow the growth of cancer cells. They work by interfering with various cellular processes essential for cancer cell survival and proliferation. Here are some examples:

Alkylating agents

These drugs add chemical groups (alkyl groups) to DNA, preventing it from replicating correctly. This leads to cell death. Example: Cisplatin

Antimetabolites

These drugs resemble essential building blocks for DNA and RNA synthesis, but they disrupt these processes when incorporated into the growing molecules. Example: Methotrexate

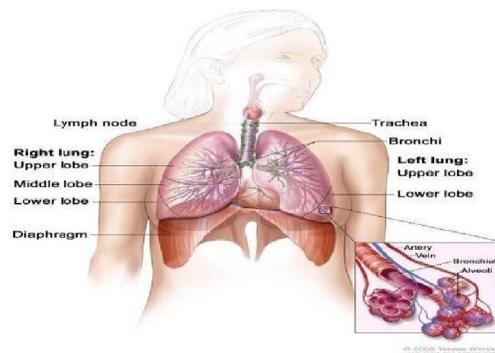
Microtubule Inhibitors

These drugs interfere with the formation and function of microtubules, essential components of the cell's internal skeleton, which are crucial for cell division. This prevents cells from dividing. Example: Vincristine

LUNG CANCER

Lung cancer is the most prevalent and deadliest type of cancer worldwide, causing nearly 1.8 million deaths annually. It is characterized by uncontrolled growth of abnormal cells in the lungs, leading to metastasis and systemic spread.

[5,6]



PATHOGENESIS OF LUNG CANCER

The pathogenesis of lung cancer is heavily influenced by genetic mutations, environmental exposures, and molecular alterations.^[7]

3.5 ADVANTAGES OF MICROSPONGES DRUG DELIVERY SYSTEM

Microsponges can absorb up to six times their weight in oil without drying out.

They provide extended drug release for up to 12 hours.

They enhance stability under chemical, physical, and thermal conditions.

They can be adapted to create innovative product shapes.

They improve patient compliance by reducing irritation and enhancing tolerance.^[8,9]

FERULIC ACID (FA)

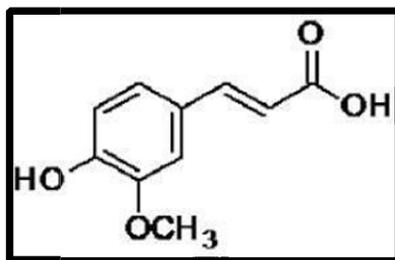
Ferulic acid, a naturally occurring phenolic acid, has attracted considerable attention as a potential anticancer agent due to its well-documented antioxidant, anti-inflammatory, and anticancer properties.

3. DRUG AND EXCIPIENT PROFILE

FERULIC ACID



Structure :

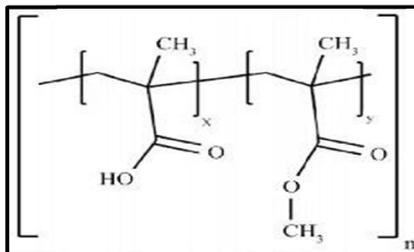


Chemical Name	: 4-Hydroxy-3-methoxycinnamic acid
Synonyms	: 4-Hydroxy-3-methoxycinnamic acid, 3-Methoxy-4hydroxycinnamic acid, Ferulic acid
IUPAC Name	: 2-(3-Hydroxy-4-methoxyphenyl)-3-propenoic acid
Molecular Formula	: C ₁₀ H ₁₀ O ₄
Molecular Weight	: 194.19 g/mol



EXCIPIENT
EUDRAGIT RL 100

Structure:



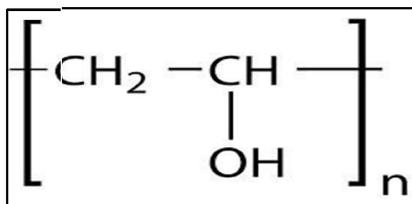
IUPAC Name	: poly (ethyl acrylate-co-methyl methacrylate-co-2-(trimethylammonio) ethyl methacrylate chloride)
Chemical Name	: Ammonio Methacrylate Copolymer Type A
Appearance	: Fine white or slightly yellowish powder
Solubility	: methanol, ethanol,
Melting Point	: 64 ⁰ - 68 ⁰ C.
Molecular weight	: 32,000g/mol.

Mechanism of action

Swelling-Controlled Diffusion

Upon contact with aqueous media, Eudragit RL 100 swells, forming a gel-like matrix. This swelling behavior allows for the controlled diffusion of encapsulated anticancer drugs. Studies have demonstrated that nanoparticles formulated with Eudragit RL 100 exhibit sustained release profiles, with cumulative drug release reaching up to 90% over an 8-hour period.

POLYVINYL ALCOHOL Structure:



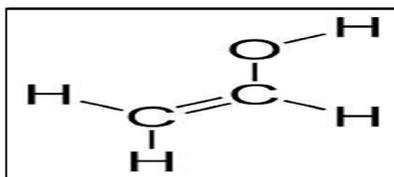
Chemical Name: Poly(2-hydroxyethylene)

Molecular Weight: Varies between 30,000 and 100,000 (dependent on degree of hydrolysis)

ETHANOL



Structure:



Chemical Name : Ethanol (C₂H₅OH)
Molecular Weight : 46.07 g/mol
Appearance : Clear, colorless, volatile liquid with a characteristic odor.
Boiling Point : 74⁰-78⁰ C
: Ethanol is miscible with water and many organic solvents. It has a high solubility for many pharmaceutical excipients and drugs, especially hydrophobic compounds.

Solubility
Density : 0.789 g/cm³
Viscosity : 1.2 mPa·s at 20°C

6. MATERIAL AND EQUIPMENTS

Table No.1: List of equipment and its manufacturers

Sr. No.	Equipments	Sources
1.	Weighing balance	Phoenix
2.	Magnetic stirrer	Remi
3.	Ultrasonicator	Wensar Electronics Pvt. Ltd., India
4.	Hot Air Oven	Biotechnics India
5.	Particle Size Analyzer (Laser Diffraction)	Litesizer Nano ZS Malvern Instruments, UK
6.	UV-Visible Spectrophotometer-1800	Shimadzu, Japan
7.	Fourier Transform Infrared Spectrometer (FTIR)	Shimadzu, Japan / Bruker, Germany



8.	Scanning Electron Microscope (SEM)	JEOL, Japan / Hitachi, Japan
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Table No. 2: List of Chemicals and its suppliers

Sr. No.	Chemicals	Sources
1.	Ferulic Acid	Otto Chemie private limited, Mumbai, India
2.	Eudragit RL100	Loba Chemie Pvt.Ltd, India
3.	Ethanol	Loba Chemie Pvt.Ltd, India
4.	Polyvinyl Alcohol	Loba Chemie Pvt.Ltd, India
5.	Distilled water	Maharashtra Scientific Emporium Wardha

7. EXPERIMENTAL WORK

Preformulation studies:

Preformulation testing is the first step in the rational development of the dosage form of the drug substance. It is defined as the investigation of the physical and chemical properties of the drug substance alone and in combination with excipients.

Organoleptic characters:

FA was tested for organoleptic properties such as colours, odour and melting point etc.

Melting point:

The melting point of FA was determined to assess its purity and confirm its identity. A small amount of the finely powdered FA sample was introduced into a capillary tube sealed at one end.

Solubility:

The solubility of FA was determined using various solvents, including water, methanol, ethanol, and phosphate buffer (pH 7.4). This data helps to select the appropriate solvent system for formulation development.

Table No.3: Excipients and its uses

Sr. No.	Ingredients	Used as
1.	Ferulic Acid	Anticancer drug
2.	Eudragit RL100	Polymer
3.	Ethanol	Solvent
4.	Polyvinyl Alcohol	Surfactant/stabilizer



5.	Distilled water	Aqueous medium
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FORMULATION OF FERULIC ACID LOADED MICROSPONGES (FA-MS)

Microsponges of FA and eudragit RL 100 was prepared by quasi-emulsion solvent diffusion method according to the formula given in table no.4. Process involved formation of quasiemulsion of two different phases

- 1.Preparation of internal phase: The phase was consisted of drug (FA), polymer (eudragit RL 100 and solvent and Ethanol 10 ml). To prepare this phase, eudragit RL 100 was dissolved in the mixture of solvents and then drug was further added to it and dissolved under under sonication
- 2.Preparation of external phase (aqueous phase): For the preparation of aqueous phase, weighed quantity of polyvinyl alcohol was taken and dissolved in 50 ml of distilled water in beaker.
- 3.Mixing: The internal organic phase was poured into the external aqueous phase by drop wise.
- 4.Stirring: The stirring was continued up to 1-2 hrs at 1000 rpm till the insoluble, rigid microparticles i.e. microsponges were formed.
- 5.Filtration: The mixture was allowed to stir until the foam settled down and after the complete evaporation of dichloromethane the mixture was filtered with whatmann filter paper (0.45 µm).
- 6.Drying: The microsponges were then dried in hot air oven at 40⁰ C.

Formulation table for FA microsponges:

Table No.4: Table revealing the master formula for FA-MS formulation.

Sr. No.	Ingredient (mg/ml/g)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1.	Ferulic acid: Eudragit RL100 (Ratio)	1:1	1:1.5	1:2	1:2.5	1:3	1:3.5	1:4	1:4.5	1:5
2.	Ferulic acid (mg)	100	100	100	100	100	100	100	100	100
3.	Eudragit RL100 (mg)	100	150	200	250	300	350	400	450	500
4.	Ethanol (ml)	10	10	10	10	10	10	10	10	10
5.	polyvinyl alcohol (mg)	300	300	300	300	300	300	300	300	300
6.	Distilled Water (ml)	50	50	50	50	50	50	50	50	50



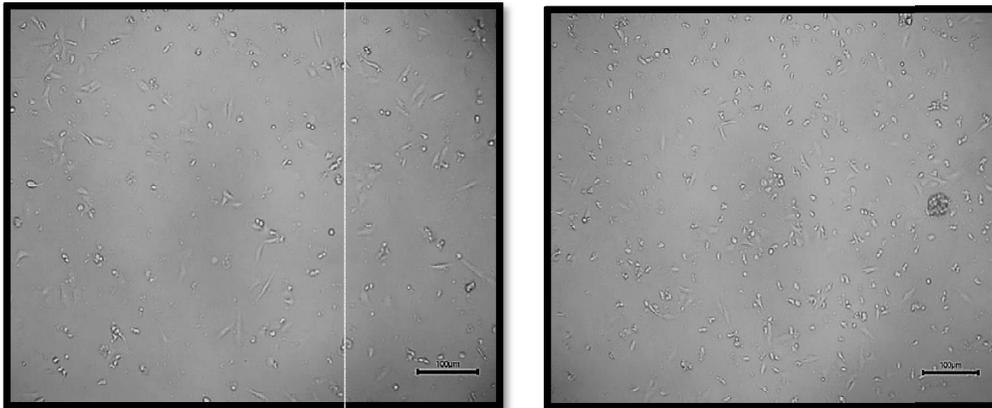


Fig.No. 27: Treated cell culture at a) 50 μm and b) 100 μm respectively

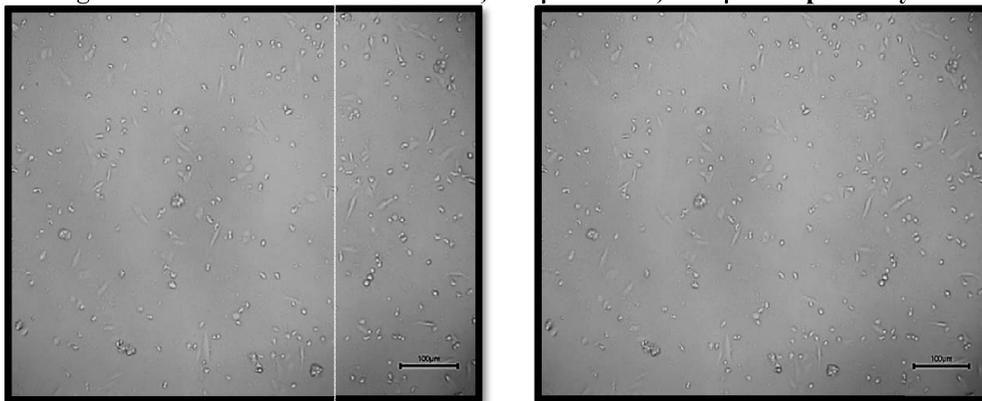
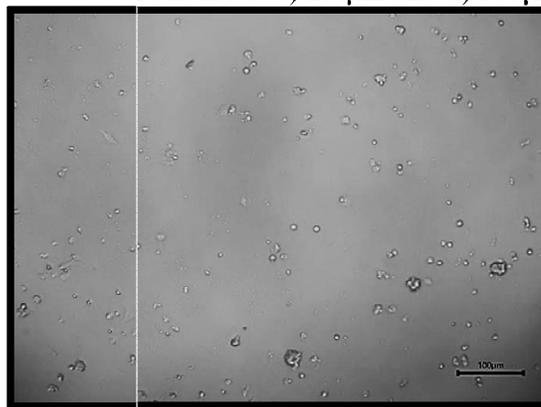


Fig.No.28: Treated cell culture at a) 250 μm and b) 500 μm respectively



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