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Research Article

Formulation and Evaluation of Oseltamivir-Loaded Microbeads

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ABSTRACT

The present study focused on the formulation and systematic evaluation of oseltamivir-loaded microbeads as a novel controlled-release drug delivery system to overcome the limitations of conventional oseltamivir administration. Oseltamivir phosphate, a potent neuraminidase inhibitor used in the treatment and prevention of influenza A and B, but suffers from challenges such as a short half-life, the need for frequent dosing, bitter taste, and poor patient compliance. To address these issues, microbeads were developed using the emulsion gelation method, employing sodium alginate as a biodegradable, biocompatible polymer and calcium chloride as a cross-linking agent. Ten formulations (F1–F10) were prepared by varying the concentration of sodium alginate, while maintaining a constant drug load. The resultant microbeads were evaluated for physicochemical and performance characteristics, including percentage yield, particle size distribution, drug content, encapsulation efficiency, swelling index at two physiological pH values (1.2 and 7.4), in vitro drug release, Fourier-transform infrared (FTIR) spectroscopy, and scanning electron microscopy (SEM). Results showed that polymer concentration had a significant impact on drug encapsulation, swelling behaviour, and release kinetics. Formulation F10 exhibited the highest encapsulation efficiency (83.12%) and swelling index, indicating enhanced mucoadhesive and controlled-release potential. Meanwhile, F1 displayed the highest drug release (96.7%) over 6 hours, making it more suitable for immediate release. FTIR analysis confirmed the chemical compatibility of oseltamivir with sodium alginate, and SEM images revealed uniform, spherical microbeads with rough surfaces, suggesting effective cross-linking and high surface area. The study concludes that oseltamivir loaded microbeads are a promising candidate for achieving sustained drug release, reduced dosing frequency, and improved patient adherence. This delivery system could be particularly beneficial in managing long-term or seasonal antiviral therapy, and may serve as an innovative platform for other short-acting antiviral drugs.

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INTRODUCTION

In pharmaceutical sciences, the form in which a drug is administered significantly impacts its therapeutic success [1]. Dosage forms act as vehicles for delivering active pharmaceutical ingredients (APIs) to the body in a safe, effective, and patient-friendly manner [2]. Conventional dosage forms such as tablets, capsules, liquids, injections, and ointments are each designed to meet specific therapeutic needs and patient populations. However, they come with limitations. Tablets and capsules, while widely used, often pose swallowing difficulties for paediatric and elderly patients and may not allow for controlled drug release [3,4]. Liquid forms can improve ease of intake but often suffer from poor stability and require preservatives. Injectables offer rapid action but are invasive and require professional administration. Semi-solid formulations like ointments are useful for topical application but provide inconsistent systemic absorption [5]. To address these challenges, pharmaceutical researchers have pursued advanced drug delivery systems that offer improved performance, sustained release, and better patient compliance [6,7,8]. Innovations such as transdermal patches, osmotic pumps, liposomes, nanoparticles, and microspheres were developed to maintain steady drug levels, minimize side effects, and reduce dosing frequency. Among these, **microbeads** have emerged as a promising and versatile technology [9,10]. Microbeads are tiny spherical structures, typically ranging from 100 to 1000 micrometres, made from biodegradable or synthetic polymers [11]. Their structure allows them to encapsulate a wide range of drugs including hydrophilic, lipophilic, and poorly soluble compounds enabling controlled or sustained release over extended periods [12,13,]. Unlike conventional drug forms that release medication in a burst, microbeads offer gradual and predictable drug delivery, helping to maintain therapeutic drug levels and improve treatment outcomes, particularly in chronic disease management [14]. Production methods such as ionotropic gelation, emulsification, spray drying, and coacervation are relatively straightforward and allow customization of bead size, surface properties, porosity, and drug release rates [15,16]. These beads not only enhance drug protection against degradation by enzymes or environmental factors like light and pH but also exhibit good flow properties and distribute uniformly in the gastrointestinal tract, leading to consistent absorption and reduced dose variability [17,18]. The origin of microbeads can be traced back to the broader development of controlled-release technologies [19].In the mid-20th century, microencapsulation was first used in industrial applications, with pharmaceutical adaptation starting in the 1960s and 1970s [20]. Early formulations focused on creating microcapsules capable of delaying drug release, which gradually evolved into modern microbeads internal drug reservoirs within polymer matrices [21,22,23]. The 1980s saw significant advancements in polymer chemistry with the emergence of safe, biodegradable polymers like PLA and PLGA, which could degrade within the body without producing harmful residues [24]. Around this time, production techniques became more refined, allowing researchers to better control bead size and release behaviour [25,26]. Their ability to encapsulate a variety of active agents and deliver them through multiple routes including oral, topical, ocular, nasal, and parenteral makes them a cornerstone of modern drug delivery science [27,28]. Though challenges remain in terms of cost, scalability, and regulatory complexity, ongoing research continues to address these limitations [29]. The demand for sustainable, biodegradable, and efficient drug delivery systems ensures that microbeads will remain central to the evolution of pharmaceutical technology [30,31].

From enhancing patient compliance to reducing side effects and enabling targeted therapy, microbeads represent a significant step forward in the development of safer, more effective, and personalized medications [32].

PREPARATION OF MICROBEADS

Materials and Methods

- **Drug:** Oseltamivir phosphate
- **Polymer:** Sodium alginate
- **Crosslinking agent:** Calcium chloride
- **Solvent:** Distilled water

Emulsion Gelation Method

Another method of Microbeads preparation is emulsion gelation techniques [33]. The sodium alginate solution was prepared by dispersing the weighed quantity of sodium alginate in deionized water. Accurately weighed quantity of drug was added to polymeric solution of Sodium alginate and drug stirred magnetically with gentle heat to get a homogenous drug polymeric mixture. Specific volume of cross-linking agent was added to form a viscous dispersion which was then extruded through a syringe with a flat tipped needle of size no. 23 magnetic stirring at 1500 rpm. The microbeads are retained in 30 min to produce rigid discrete particles. They were collected by decantation and the products thus separated was washed with chloroform to remove the traces on microbeads were dried [34,35,].

Table:1 Formulations code for formulation of Oseltamivir-loaded Microbeads

Formulation Code	Sodium Alginate	Water	Calcium Chloride	Drug
F1	0.5 g	50 ml	50 ml	1 g
F2	1.0 g	50 ml	50 ml	1 g
F3	1.5 g	50 ml	50 ml	1 g
F4	2.0 g	50 ml	50 ml	1 g
F5	2.5 g	50 ml	50 ml	1 g
F6	3.0 g	50 ml	50 ml	1 g
F7	3.5 g	50 ml	50 ml	1 g
F8	4.0 g	50 ml	50 ml	1 g
F9	4.5 g	50 ml	50 ml	1 g
F10	5.0 g	50 ml	50 ml	1 g

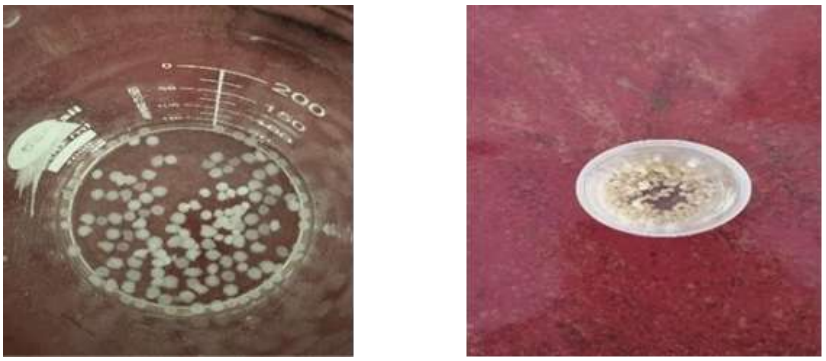

Fig.6.1 Images of Oseltamivir-loaded Microbeads

EVALUATION STUDIES

1. **Percentage yield**

Percentage yield is a key parameter used to determine the efficiency of the microbead formulation process [36].

Percentage Yield (%) = (Practical yield / Theoretical yield) × 100

2. Particle Size and Size Distribution

Purpose: To determine average size of microbeads and ensure uniformity [37].

3. Drug Content (Drug Loading)

To quantify how much drug is loaded in the microbeads.

Drug Content (%) = (Amount of drug in microbeads / Total weight of microbeads) × 100

4. Percentage Encapsulation Efficiency (%EE)

To Measures how much drug is actually trapped inside the microbeads.

Formula: EE (%) = (Amount of drug encapsulated / Total amount of drug used) × 100 [38].

5. Swelling Index

Purpose: To evaluate the swelling behaviour in different pH environments

Formula: Swelling Index = (Wg / Wo) x 100

Wg = weight of dry microbeads, Wo = weight of wet microbeads [39].

6. Scanning Electron Microscopy (SEM)

It is a type of electron microscope that uses a focused beam of high-energy electrons to scan the surface of a specimen [40].

7. Evaluate In vitro drug release studies

In vitro drug release refers to how much drug is released from the microbeads into a liquid medium (usually phosphate buffer pH 7.4) under lab conditions

% Drug Release = (Amount of drug released at a time point / Total amount of drug in microbeads) × 100 [41,42,43,44].

How was the Study Done? (Standard procedure)

- Medium: Phosphate buffer (pH 7.4), 900 mL
- Temperature: 37 ± 0.5 °C (to match body temp)
- Apparatus: USP Dissolution Apparatus
- Speed: 100 rpm and Time Points: 0.5, 1, 2, 3, 4, 5, and 6 hours
- Sample withdrawn at each time point and analysed using UV spectrophotometry at appropriate λmax-220 to 240[45].

8. Fourier Transform Infrared Spectroscopy (FTIR)

The purpose of Fourier Transform Infrared Spectroscopy (FTIR) is to identify and analyse the chemical structure of substances by detecting the specific functional groups present in a molecule [46,47]. It helps in determining the composition, purity, and molecular interactions within a sample. In pharmaceutical applications, FTIR is mainly used to confirm the identity of drugs, detect any possible interactions between drug and excipients, and ensure the stability and compatibility of formulations such as microbeads. It is a valuable tool for both research and quality control purposes [48].

RESULTS

Table 2: Practical Yield and Percentage Yield of Formulations (F1-F10)

Formulation code	Sodium Alginate (g)	Oseltamivir Drug (g)	Theoretical Yield (g)	Practical Yield (g)	Percentage Yield (%)
F1	0.5	1	1.5	1.38	92.00%
F2	1.0	1	2.0	1.42	71.00%
F3	1.5	1	2.5	1.44	57.60%
F4	2.0	1	3.0	1.40	46.66%
F5	2.5	1	3.5	1.35	38.57%
F6	3.0	1	4.0	1.30	32.50%
F7	3.5	1	4.5	1.27	28.22%
F8	4.0	1	5.0	1.25	25.00%
F9	4.5	1	5.5	1.23	22.36%
F10	5.0	1	6.0	1.20	20.00%

Table 3: Evaluation parameter of Oseltamivir-loaded microbeads

Formulation code	Particle Size µm	Swelling Index (pH 1.2)	Swelling Index (pH 7.4)	Encapsulation Efficiency %	Drug content (%)
F1	410 µm	280.21	498.37	42.35	29.65
F2	452 µm	296.48	521.22	47.82	27.88
F3	479 µm	312.92	544.10	52.16	26.14
F4	510 µm	336.11	567.03	58.02	24.62
F5	534 µm	359.20	591.47	63.17	22.89
F6	556 µm	382.89	615.75	68.35	21.08
F7	583 µm	407.32	640.84	72.49	19.83
F8	601µm	429.16	666.29	76.70	18.76
F9	625 µm	450.72	691.83	79.88	17.65
F10	641 µm	472.44	696.41	83.12	16.45

SEM Photograph of Oseltamivir-loaded Microbeads

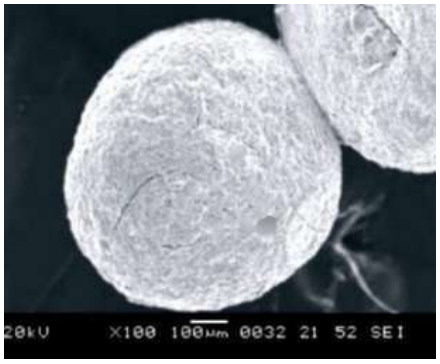

Fig2: SEM Photograph of Oseltamivir-loaded microbeads

The SEM image of Oseltamivir-loaded microbeads at 100× magnification shows nearly spherical particles with a rough and porous surface. The roughness may enhance drug release by increasing the surface area. The absence of aggregation and uniform size distribution suggest successful emulsification and crosslinking. Minor surface cracks could be attributed to polymer shrinkage during drying [49,50].

In vitro drug release studies result:

Table 4: In vitro drug release percentage studies

Time (hrs)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)	F6 (%)	F7 (%)	F8 (%)	F9 (%)	F10 (%)
0.5	22.4	20.2	18.7	17.1	16.5	15.4	14.7	14.1	13.4	12.6
1	38.2	35.5	33.0	30.7	29.4	28.0	27.1	26.3	25.2	24.0
2	55.6	52.1	48.7	45.3	43.8	42.0	40.9	39.7	38.5	36.8

3	67.4	64.1	61.3	58.0	56.2	54.6	52.7	51.3	49.9	48.0
4	79.1	75.3	72.5	69.0	67.4	65.8	63.9	62.4	60.3	58.4
5	90.2	87.1	84.0	81.5	79.0	77.1	74.5	73.0	71.2	69.1
6	96.7	94.0	91.3	89.1	87.0	85.1	82.9	81.0	79.1	76.5

Graphical representation of In vitro drug release of Oseltamivir-loaded Microbeads

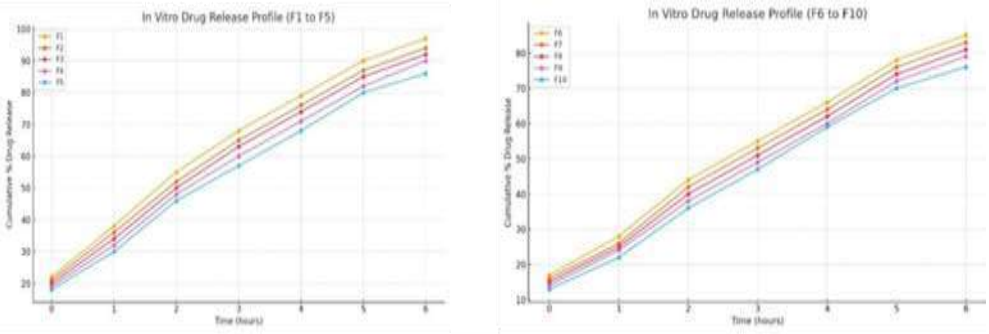

Fig 3: Graphical representation of In vitro drug release of Oseltamivir-loaded Microbeads

Fourier Transform Infrared Spectroscopy (FTIR) of Oseltamivir Drug

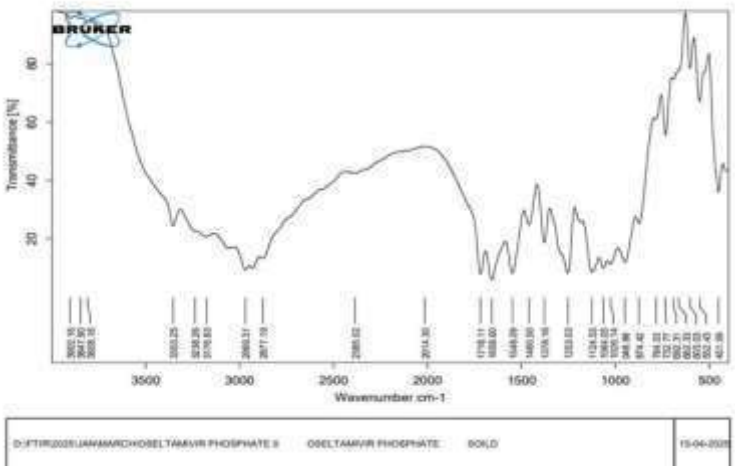

Fig 4: IR Spectrum of the Oseltamivir phosphate drug

Table 5: FTIR Interpretation of Oseltamivir Phosphate

Wavenumber (cm^{-1})	Peak Assignment	Functional Group
3390–3180	Broad strong band	O–H and N–H stretching (alcohols, amines)
2950–2850	Medium peaks	C–H stretching (aliphatic CH_3, CH_2)
1730–1700	Sharp peak (around 1718)	C=O stretching (ester or carboxylic acid)
1640–1550	Medium band (around 1568, 1540)	N–H bending or C=C stretching (amide or aromatic ring)
1450–1350	Peaks around 1380	C–H bending (CH_3, CH_2 groups)
1250–1000	Strong multiple bands (1024–1124 cm^{-1})	C–O–C and C–N stretching (ether and amine groups)
900–650	Peaks around 894, 782, 722 cm^{-1}	Aromatic C–H bending or phosphate vibrations
~500–450	Low intense peaks	Out-of-plane bending (fingerprint region)

Fourier Transform Infrared Spectroscopy (FTIR) of Sodium alginate

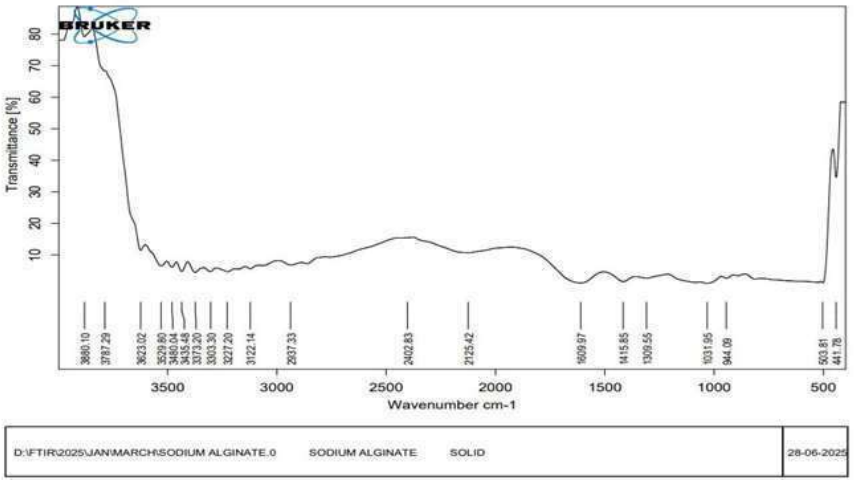

Fig 5: IR Spectrum of the Sodium alginate

Table 6: FTIR Interpretation of Sodium Alginate

Wavenumber (cm^{-1})	Peak Assignment	Functional Group
3289.02 – 3239.26	O–H stretching (broad)	Hydroxyl (–OH)
2927.33	C–H stretching	Alkanes
2165.42	C≡C stretching	Alkyne (possible)
1609.97	Asymmetric COO^- stretching	Carboxylate salt
1415.65	Symmetric COO^- stretching	Carboxylate salt
1031.95 – 944.09	C–O–C stretching (pyranose ring)	Ether / Polysaccharide
503.81 – 441.78	Fingerprint region	Polymer backbone bending

Fourier Transform Infrared Spectroscopy (FTIR)

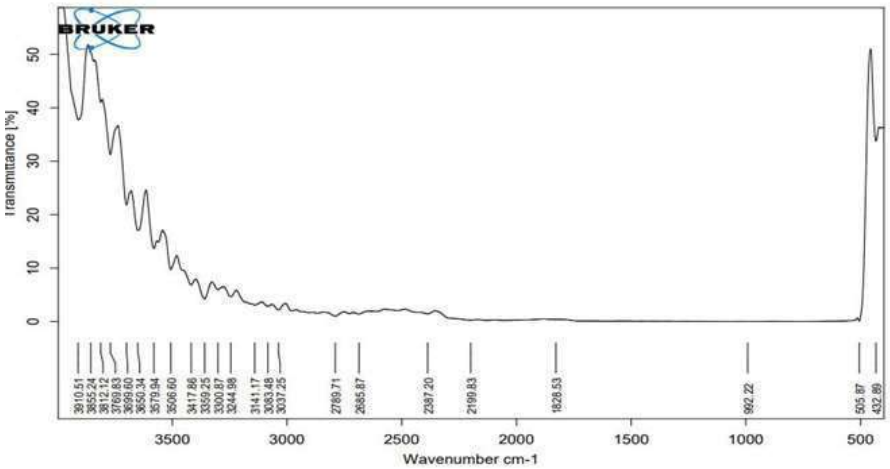

Fig 6: IR Spectrum of the Oseltamivir-loaded microbeads

Table 7: FTIR Interpretation of Oseltamivir-Loaded Microbeads

Wavenumber (cm^{-1})	Peak Assignment	Functional Group
3285.87 – 3235.69	O–H stretching (broad)	Hydroxyl (–OH, from alginate)
2926.20 – 2878.97	C–H stretching	Alkanes
2199.83	Minor shift, possible C≡C stretching	Alkyne (weak)
1826.53	C=O stretching (broad overlap)	Ester / Carboxylate
1298.43 – 1030.25	C–O stretching	Ether, Ester
992.22	=C–H bending	Alkene or aromatic bending
505.87 – 425.89	Fingerprint region	Crosslinking vibrations

CONCLUSION

This study successfully developed oseltamivir-loaded microbeads using sodium alginate via the emulsion gelation method. Increasing polymer concentration led to larger particle sizes, higher swelling indices at both pH 1.2 and 7.4, and improved encapsulation efficiency (up to 83.12% in F10), enhancing the system's potential for targeted intestinal release. Although drug content decreased with higher polymer levels, this supported a sustained release profile, with F10 showing the slowest release (76.5%) over six hours. SEM analysis confirmed spherical, porous microbeads, and FTIR revealed no significant drug-excipient interactions. Formulation F10 was identified as the most optimized for controlled and targeted antiviral drug delivery.

CONFLICT OF INTEREST:

The Authors declares of No Conflict of interest.

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