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Preparation and Characterization of Mucoadhesive Microspheres Containing Antidiabetic Agent

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Abstract: *The study focuses on the preparation and evaluation of gliclazide-loaded microspheres using two distinct methods: Ionic Orifice Gelation and Emulsification Ionic Gelation. Various natural gums, including gum kondagogu, xanthan gum, and guar gum, were used as mucoadhesive polymers in different ratios with sodium alginate. Microspheres were characterized for particle size, angle of repose, microencapsulation efficiency, FT-IR, and in vitro drug release profiles. FT-IR and XRD analyses indicated significant interactions between gliclazide and the excipients, impacting the drug's crystallinity and dissolution behavior. Scanning Electron Microscopy (SEM) revealed that microspheres prepared via Ionic Orifice Gelation exhibited more uniform and spherical morphology compared to those prepared by Emulsification Ionic Gelation. Physical properties such as angle of repose, bulk density, Carr's index, Hausner's ratio, true density, and average particle size were assessed, showing differences in flowability and compressibility between formulations. The drug content and encapsulation efficiency varied, highlighting the importance of formulation parameters. In vitro release studies demonstrated that the microspheres could sustain drug release over an extended period, making them suitable for controlled drug delivery. The study concludes that the Ionic Orifice Gelation technique is superior for producing uniform microspheres with desirable physical properties and controlled drug release characteristics.*

Keywords: Gliclazide, Microspheres, Ionic Orifice Gelation, Emulsification Ionic Gelation, Sodium Alginate, Natural Gums, Mucoadhesive Polymers, Controlled Drug Delivery, FT-IR Analysis.

I. INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia, resulting from defects in insulin secretion, insulin action, or both. Among the therapeutic options available, oral hypoglycemic agents such as sulfonylureas play a critical role in managing type 2 diabetes. Gliclazide, a second-generation sulfonylurea, is widely used due to its efficacy in controlling blood glucose levels by stimulating insulin secretion from pancreatic β-cells. However, the conventional dosage forms of gliclazide present several limitations, including poor bioavailability, frequent dosing, and associated side effects such as hypoglycemia.

To overcome these challenges, the development of controlled release drug delivery systems has gained significant attention. Microspheres, in particular, offer a promising approach due to their ability to provide sustained and controlled release of drugs, enhance bioavailability, reduce dosing frequency, and minimize side effects. Microspheres are spherical, free-flowing particles ranging in size from 1 to 1000 micrometers, and they can be formulated using various natural and synthetic polymers.

In this study, we focus on the development and characterization of gliclazide-loaded microspheres using ethyl cellulose as the polymer matrix. Ethyl cellulose is a widely used biocompatible polymer known for its excellent film-forming properties, stability, and ability to control drug release. By encapsulating gliclazide in ethyl cellulose microspheres, we aim to achieve a controlled release profile, thereby improving therapeutic efficacy and patient compliance.

The objectives of this research are to:

Formulate gliclazide-loaded microspheres using the solvent evaporation technique.

Characterize the prepared microspheres in terms of particle size, morphology, encapsulation efficiency, and drug release profile.

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Evaluate the in vitro release kinetics of gliclazide from the microspheres to determine the most suitable formulation for sustained release.

This study not only addresses the challenges associated with conventional gliclazide therapy but also contributes to the growing body of knowledge on the design and application of controlled release drug delivery systems. Through meticulous formulation and evaluation, we aim to develop a microsphere-based delivery system that offers significant advantages over existing dosage forms, ultimately improving the management of type 2 diabetes.

II. MATERIALS AND METHOD

Microspheres of gliclazide were prepared by two methods: Ionic orifice gelation technique and Emulsification ionic gelation technique

Orifice Ionic Gelation Technique

Gliclazide microspheres were prepared by using different ratios of drug: Sod. Alginate: natural gum as mucoadhesive polymer at concentrations (1:1:0.25, 1:1:0.5, 1:1:0.75, 1:1:1) with every gum (gum kondagogu, gum Xanthan, gum guar) and the batches were named as (OMK1, OMK2, OMK3, OMK4), (OMX1, OMX2, OMX3, OMX4) and (OMG1, OMG2, OMG3, OMG4). The pure drug is dispersed in the solution of sodium alginate and water and to this; the gum was added and stirred to get a viscous aqueous dispersion. Drop wisely the dispersion was extruded through 22# syringe needle and poured in 15% CaCl2 solution by stirring at 50 rpm using a magnetic stirrer (Remi MS-301). The microspheres thus formed are allowed 30min for curing in calcium chloride solution then were decanted and washed with petroleum ether and air dried over night at room temperature.

Emulsification Ionic Gelation Technique

Gliclazide microspheres were prepared by using different ratios of drug: Sod. Alginate: natural gum as mucoadhesive polymer at concentrations (1:1:0.25, 1:1:0.5, 1:1:0.75, 1:1:1) with every gum (gum kondagogu, gum Xanthan, gum guar) and the batches were named as (EMK1, EMK2, EMK3, EMK4), (EMX1, EMX2, EMX3, EMX4) and (EMG1, EMG2, EMG3, EMG4). The pure drug is dispersed in the solution of sodium alginate and water and to this, the gum was added and stirred to get a viscous aqueous dispersion which was then extruded through a syringe needle 23# into light liquid paraffin containing 1.5% span-80 and 0.2% glacial acetic acid being kept under magnetic stirring (Remi MS-301) at 500 rpm to undergo emulsification which then leads to form spheres dispersed. Needed amount of 15% w/v calcium chloride solution is poured by continuing stirring, by which the formed spheres are exposed towards the calcium chloride. The formed spheres were allowed to keep as such for 30minutes to finish curing process. The microspheres were decanted and washed with petroleum ether to remove liquid paraffin and water. They were collected by decantation and the product thus separated was washed with chloroform to remove the traces of paraffin oil and dried

III. EVALUATION OF MICROSPHERES

Particle Size Analysis

Angle of Repose

Microencapsulation Efficiency

FT-IR Studies Fourier Transform Infrared Analysis (FT-IR) [140,141]

% Drug Content Evaluation

Microspheres equivalent to 80mg of gliclazide were crushed in a mortar and extracted with 10ml of methanol then volume adjusted up to 100ml with 6.8 pH phosphate buffer. 1ml of the aliquot was taken and made up to the volume 10ml with phosphate buffer 6.8 pH and absorbance was measured at ⱷmax 229 nm using UV visible spectrophotometer (Schimazdu UV1700-E23). The procedure was repeated with pure gliclazide and %drug content is calculated.

In vitro Wash-Off Test for Mucoadhesive Microspheres

A piece of intestinal mucosa (2x2 cm) was mounted on to glass slide of (3x1 inch) using elastic bands. About 50 microspheres were spread on each wet tissue specimen and then the slide was hung on to the arm of a USP tablet disintegrating test apparatus. The disintegration machine containing tissue specimen was adjusted for up and down

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moment in 6.8pH phosphate buffer at 37oC in a beaker. Number of microspheres still adhering on to the tissue was counted at hourly intervals up to 8 hr

In vitro Release Studies

Microspheres equivalent to 80mg gliclazide were packed in hard gelatin capsules and subjected to in vitro drug release studies in 0.1N HCl for first two hours and then transferred into pH 6.8 phosphate buffer (900ml) using USP XXIV eight-station dissolution test apparatus (Electrolab ETD-209) with a basket stirrer at 100 rpm at 37 ± 0.5°C for 12hrs. Samples were withdrawn at predetermined time intervals and analyzed by UV-spectroscopy at ⱷmax 227nm (0.1N HCl) & 229nm (pH 6.8 phosphate buffer). The data used to determine rate, order and mechanism of drug release

IV. RESULTS

FTIR

In the FTIR analysis (Fig 7.1), the overlay spectra of gliclazide in its pure form and when combined with sodium alginate and natural gums reveal significant shifts and intensity variations in the characteristic peaks. Upon comparison, it's evident that certain peaks exhibit alterations in their positions and intensities, indicating potential interactions between gliclazide and the excipients. These alterations suggest the formation of new chemical bonds or changes in molecular conformation due to interactions with the polymer matrix. Such interactions could influence the dissolution behavior, stability, and bioavailability of the gliclazide formulation.

Furthermore, the XRD analysis (Fig 7.2) provides insights into the crystalline structure of gliclazide when formulated with sodium alginate and natural gums. The overlay spectra reveal changes in the diffraction patterns and peak intensities compared to the pure drug. These changes may indicate modifications in the crystallinity of gliclazide due to interactions with the excipients. The presence of excipients such as sodium alginate and natural gums could potentially disrupt the crystalline lattice of gliclazide, leading to reduced crystallinity or the formation of new crystalline phases. Such alterations in crystallinity could impact the drug's dissolution rate and overall performance in pharmaceutical formulations.

Overall, the FTIR and XRD analyses provide valuable information about the interactions between gliclazide and the excipients, shedding light on the potential changes in molecular structure and crystallinity induced by formulation with sodium alginate and natural gums. These findings underscore the importance of understanding the physicochemical properties of drug-excipient interactions in pharmaceutical formulations to optimize drug delivery systems and ensure product efficacy and stability. Further studies could focus on elucidating the specific mechanisms underlying these interactions and their implications for drug formulation and performance.

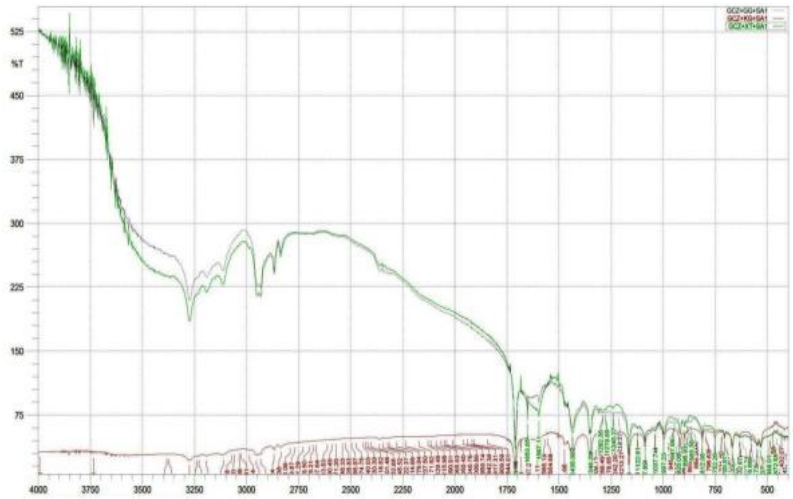

Fig 1: FTIR overlay spectra of gliclazide pure drug and gliclazide with sodium alginate and natural gums.

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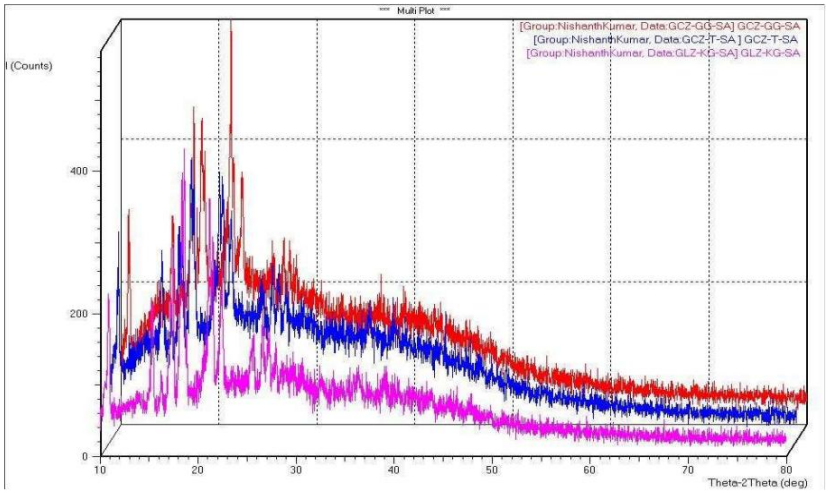

Fig 2: XRD overlay spectra of pure drug gliclazide and gliclazide with sodium alginate and natural gums

SEM Pictograms of gliclazide microcapsules formulated with xanthan gum by Ionic orifice Gelation Technique and Emulsion Ionic gelation techniques.

Fig 7.3 presents scanning electron microscope (SEM) images depicting gliclazide microcapsules formulated with xanthan gum using two different techniques: Ionic Orifice Gelation (IOG) and Emulsion Ionic Gelation (EIG).

In the SEM images, microcapsules formulated via the Ionic Orifice Gelation (IOG) technique exhibit a uniform and spherical morphology, with smooth surfaces and well-defined boundaries. The microcapsules appear to have a relatively consistent size distribution, indicating controlled encapsulation of gliclazide within the xanthan gum matrix. This suggests that the IOG technique facilitates precise control over the size and morphology of the microcapsules, potentially enhancing drug release kinetics and bioavailability.

Conversely, microcapsules prepared using the Emulsion Ionic Gelation (EIG) technique display a more irregular and heterogeneous morphology compared to those produced by IOG. The microcapsules exhibit varying sizes and shapes, with some appearing more elongated or deformed. Additionally, the surfaces of the microcapsules appear rougher and less uniform, possibly due to differences in the emulsification and gelation processes involved in the EIG technique. Despite these variations, the microcapsules still demonstrate encapsulation of gliclazide within the xanthan gum matrix, albeit with less uniformity compared to IOG.

Overall, the SEM images provide visual insights into the morphological characteristics of gliclazide microcapsules formulated with xanthan gum using different encapsulation techniques. While both IOG and EIG methods are capable of encapsulating gliclazide within xanthan gum microcapsules, the IOG technique appears to yield more uniform and well-defined microcapsules compared to EIG. These observations underscore the importance of selecting an appropriate encapsulation technique to achieve desired microcapsule morphology and optimize drug delivery characteristics. Further studies could explore the influence of formulation parameters and process conditions on microcapsule morphology and drug release behavior to enhance the performance of xanthan gum-based microcapsule formulations for pharmaceutical applications.

Physical properties of gliclazide microspheres formulated with natural gums by Orifice ionic gelation technique.

The physical properties of gliclazide microspheres formulated with natural gums using the Orifice Ionic Gelation technique, as presented in Table 7.1, provide valuable insights into the characteristics of these microspheres. Let's delve into a detailed explanation of these properties:

Angle of Repose: This parameter measures the flowability of the microspheres. A lower angle of repose indicates better flow properties. Formulation OMK2 exhibited the highest angle of repose (26.3° ± 0.72), suggesting slightly poorer flow characteristics compared to other formulations.

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Bulk Density: Bulk density is a measure of the compactness of the microspheres. Higher bulk density values imply greater compactness. Formulation OMK1 demonstrated the highest bulk density (0.66 g/cm³ ± 0.03), indicating higher packing efficiency.

Carr's Index: Carr's index provides insight into the compressibility of the microspheres. Lower Carr's index values indicate better flow properties and compressibility. Formulation OMK3 had the highest Carr's index (96.68% ± 0.56), suggesting slightly poorer compressibility compared to other formulations.

Hausner's Ratio: Hausner's ratio is another measure of the flowability and compressibility of the microspheres. Lower values indicate better flow properties and compressibility. Most formulations exhibited Hausner's ratios close to 0.04, indicating good flow characteristics.

True Density: True density represents the density of the material without any void spaces. Formulation OMX1 had the lowest true density (0.79 g/cm³ ± 0.4), indicating the presence of more void spaces within the microspheres.

Average Particle Size: The average particle size is crucial for determining the size distribution and surface area of the microspheres. Formulation OMX4 exhibited the largest average particle size (555 µm ± 5), indicating a broader size distribution compared to other formulations.

Overall, these physical properties collectively indicate the flowability, compressibility, and particle size distribution of the gliclazide microspheres formulated with natural gums using the Orifice Ionic Gelation technique. Formulations with lower angles of repose, higher bulk densities, and lower Carr's index values generally demonstrate better flow properties and compressibility, which are desirable for pharmaceutical applications such as encapsulation and controlled release.

Table 1: Physical properties of gliclazide microspheres by Orifice ionic gelation technique.

Sl. no	Formulation code	Angle of repose	Bulk density (g/cm3)	Carr's index	Hausner's ratio	True density (g/cm3)	Average particle size
1	OMK1	25.4±0.61	0.66±0.03	96.46±0.31	0.04	0.90±0.2	420±10
2	OMK2	26.3±0.72	0.63±0.04	96.35±0.46	0.04	0.96±0.4	460±18
3	OMK3	26.5±0.81	0.56±0.05	96.68±0.56	0.03	0.92±0.5	480±20
4	OMK4	25.3±0.73	0.64±0.06	96.28±0.51	0.04	0.94±0.3	485±10
5	OMG1	24.6±0.91	0.60±0.03	96.63±0.49	0.03	0.83±0.5	500±5
6	OMG2	25.2±0.63	0.55±0.02	96.39±0.59	0.04	0.91±0.2	515±6
7	OMG3	24.8±0.74	0.57±0.09	96.25±0.41	0.04	0.93±0.3	525±8
8	OMG4	24.3±0.91	0.62±0.06	96.34±0.51	0.03	0.89±0.1	530±10
9	OMX1	25.7±0.84	0.61±0.04	96.93±0.41	0.04	0.79±0.4	525±5
10	OMX2	23.2±0.91	0.66±0.06	96.25±0.49	0.03	0.87±0.5	534±8
11	OMX3	25.6±0.71	0.56±0.04	96.33±0.65	0.04	0.94±0.2	545±10
12	OMX4	24.8±0.82	0.59±0.05	96.13±0.51	0.04	0.96±0.1	555±5

Physical properties of gliclazide microspheres formulated with natural gums by Emulsion ionic gelation technique.

The physical properties of gliclazide microspheres formulated with natural gums using the Emulsion Ionic Gelation technique, as presented in Table 7.2, provide important insights into their characteristics. Let's discuss these properties in detail:

Angle of Repose: This parameter reflects the flowability of the microspheres. A lower angle of repose indicates better flow properties. The formulations in this table exhibit angle of repose values ranging from 23.2° to 27.2°. Among them, EMX2 demonstrated the lowest angle of repose (23.2° ± 0.61), suggesting excellent flow characteristics.

Bulk Density: Bulk density is a measure of the compactness of the microspheres. Higher bulk density values indicate greater compactness. Formulation EMX2 exhibited the highest bulk density (0.68 g/cm³ ± 0.06), indicating efficient packing of particles.

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Carr's Index: Carr's index provides insights into the compressibility of the microspheres. Lower Carr's index values suggest better flow properties and compressibility. The formulations in this table showed Carr's index values ranging from 96.15% to 96.63%. EMX4 had the lowest Carr's index (96.15% ± 0.51), indicating good compressibility.

Hausner's Ratio: Hausner's ratio is another indicator of the flowability and compressibility of the microspheres. Lower values suggest better flow properties and compressibility. Most formulations exhibited Hausner's ratios close to 0.04, indicating good flow characteristics.

True Density: True density represents the density of the material without any void spaces. The true density values for the formulations ranged from 0.79 g/cm³ to 0.96 g/cm³. EMX1 had the lowest true density (0.79 g/cm³ ± 0.4), indicating the presence of void spaces within the microspheres.

Average Particle Size: The average particle size is crucial for determining the size distribution and surface area of the microspheres. The formulations in this table exhibited average particle sizes ranging from 490 µm to 530 µm. EMK3 had the largest average particle size (530 µm ± 8), indicating a broader size distribution.

The formulations with lower angles of repose, higher bulk densities, lower Carr's index values, and smaller average particle sizes generally exhibit better flow properties, compressibility, and particle size distribution, which are desirable for various pharmaceutical applications.

Table 2: Physical properties of gliclazide microspheres by Emulsion ionic gelation technique.

Sl. no	Formulation code	Angle of repose	Bulk density (g/cm3)	Carr's index	Hausner's ratio	True density (g/cm3)	Average particle size
1	EMK1	25.4±0.61	0.66±0.03	96.46±0.31	0.04	0.90±0.2	490±10
2	EMK2	26.3±0.72	0.63±0.04	96.38±0.46	0.04	0.96±0.4	510±5
3	EMK3	27.2±0.52	0.56±0.05	96.58±0.34	0.03	0.92±0.5	530±8
4	EMK4	25.3±0.73	0.64±0.06	96.28±0.51	0.04	0.94±0.3	528±5
5	EMG1	24.6±0.91	0.60±0.03	96.63±0.49	0.03	0.82±0.5	510±10
6	EMG2	25.2±0.63	0.56±0.04	96.39±0.59	0.04	0.91±0.2	525±5
7	EMG3	24.8±0.74	0.57±0.09	96.25±0.41	0.04	0.93±0.3	528±8
8	EMG4	24.3±0.91	0.60±0.07	96.34±0.51	0.03	0.89±0.1	531±6
9	EMX1	25.7±.0.84	0.61±0.04	96.58±0.43	0.04	0.79±0.4	500±10
10	EMX2	23.2±0.61	0.68±0.06	96.25±0.49	0.03	0.87±0.5	498±12
11	EMX3	25.6±0.71	0.56±0.04	96.33±0.65	0.04	0.94±0.2	506±10
12	EMX4	24.8±0.82	0.59±0.05	96.15±0.51	0.04	0.96±0.1	512±8

% Drug content and encapsulation efficiency of microspheres prepared by orifice ionic gelation technique

Table 3: % Drug content and encapsulation efficiency by orifice ionic gelation technique

Sl. No	Formulation code	D/P ratio	% Drug content	Encapsulation efficiency (%)
1	OMG1	1:0.25	31.91±0.64	72.05±0.48
2	OMG2	1:0.5	28.03±0.68	70.05±0.51
3	OMG3	1:.75	24.63±0.58	67.79±0.83
4	OMG4	1:1	23.11±0.56	69.33±0.40
5	OMX1	1:0.25	29.09±0.85	60.69±0.53
6	OMX2	1:0.5	23.04±0.79	57.50±0.59
7	OMX3	1:.75	21.37±0.68	58.80±0.41
8	OMX4	1:1	19.96±0.48	59.90±0.43
9	OMK1	1:0.25	26.32±0.56	59.22±0.61

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10	OMK2	1:0.5	22.48±0.57	56.21±0.52
11	OMK3	1:.75	20.02±0.59	55.09±0.56
12	OMK4	1:1	19.50±0.62	55.89±0.51

% Drug content and encapsulation efficiency of microspheres prepared by emulsion ionic gelation technique.

The provided table presents the % drug content and encapsulation efficiency of microspheres prepared by the emulsion ionic gelation technique. Let's discuss these parameters:

D/P Ratio: The D/P ratio represents the ratio of the drug (D) to the polymer (P) used in the formulation. It indicates the amount of drug relative to the polymer in the microspheres. In this table, different formulations have been prepared with varying D/P ratios, ranging from 1:0.25 to 1:1.

% Drug Content: This parameter represents the percentage of the actual drug content in the microspheres relative to the total weight of the microspheres. It provides information about the efficiency of drug incorporation into the microspheres during the formulation process. The % drug content values range from 20.08% to 32.15%.

Encapsulation Efficiency: Encapsulation efficiency refers to the percentage of drug encapsulated within the microspheres relative to the total amount of drug used in the formulation. It indicates the effectiveness of the formulation process in retaining the drug within the microspheres. The encapsulation efficiency values range from 56.09% to 72.55%.

These parameters are crucial indicators of the quality and performance of the microsphere formulations. A higher % drug content and encapsulation efficiency suggest better drug-loading capacity and retention within the microspheres, which are desirable attributes for controlled drug delivery systems.

The variations observed in % drug content and encapsulation efficiency among different formulations may be attributed to differences in formulation parameters such as polymer concentration, drug-polymer ratio, emulsification technique, and processing conditions. Optimization of these parameters is essential to achieve desired drug-loading capacity and encapsulation efficiency while ensuring uniformity and stability of the microsphere formulations.

Table 4: % Drug content and encapsulation efficiency of emulsion ionic gelation technique.

Sl. No	Formulation code	D/P ratio	% Drug content	Encapsulation efficiency (%)
1	EMG1	1:0.25	32.15±0.54	72.55±0.58
2	EMG2	1:0.5	28.83±0.48	71.05±0.41
3	EMG3	1:.75	25.13±0.68	68.73±0.63
4	EMG4	1:1	24.21±0.46	70.33±0.50
5	EMX1	1:0.25	30.09±0.65	61.68±0.43
6	EMX2	1:0.5	24.04±0.49	58.5±0.69
7	EMX3	1:.75	22.37±0.58	59.8±0.51
8	EMX4	1:1	20.96±0.68	60.9±0.63
9	EMK1	1:0.25	27.32±0.76	59.82±0.41
10	EMK2	1:0.5	23.48±0.57	58.2±0.62
11	EMK3	1:.75	20.08±0.49	56.09±0.86
12	EMK4	1:1	21.50±0.55	57.89±0.61

Wall thickness, release rate constant and permeability coefficient of microspheres prepared by orifice ionic gelation technique.

The provided table contains important parameters such as wall thickness, release rate constant, and permeability coefficient of microspheres prepared by the orifice ionic gelation technique. Let's discuss these parameters:

Wall Thickness: This parameter represents the thickness of the microsphere shell, which is crucial for controlling drug release kinetics. The formulations exhibit wall thickness values ranging from 3.68 µm to 5.98 µm. Among them,

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formulation OMG1 has the highest wall thickness (5.98 µm ± 0.34), while formulation OMX4 has the lowest (3.68 µm ± 0.51).

Release Rate Constant (mg/hr): The release rate constant determines the rate at which the drug is released from the microspheres over time. It represents the slope of the release curve and indicates the extent of drug release. The formulations demonstrate release rate constants ranging from 0.9561 mg/hr to 0.9922 mg/hr. The release rate constant reflects the intrinsic properties of the microspheres and the drug formulation.

Permeability Coefficient: The permeability coefficient represents the ability of the drug to pass through the microsphere shell. It is a measure of the diffusion rate of the drug through the polymeric matrix. The formulations in the table exhibit permeability coefficients ranging from 4.067 to 5.875. A higher permeability coefficient indicates faster drug release due to increased drug diffusion through the microsphere shell.

Overall, these parameters provide valuable insights into the characteristics and behavior of the microspheres prepared by the orifice ionic gelation technique. The variations observed in wall thickness, release rate constant, and permeability coefficient among different formulations can influence the drug release profile and ultimately affect the therapeutic efficacy of the microsphere-based drug delivery system.

Table 5: Wall thickness, release rate constant and permeability coefficient of microspheres prepared by orifice ionic gelation technique.

Sl. No	Formulation code	Wall thickness (µ)	Release rate constant (mg/hr)	Permeability coefficient
1	OMG1	5.98±0.34	0.9824	5.875
2	OMG2	5.138±0.56	0.9922	5.098
3	OMG3	4.23±0.49	0.9816	4.152
4	OMG4	3.68±0.51	0.9917	4.403
5	OMX1	5.65±0.49	0.9871	5.577
6	OMX2	5.42±0.51	0.9901	5.366
7	OMX3	4.65±0.41	0.9872	4.590
8	OMX4	4.12±0.46	0.9872	4.067
9	OMK1	4.85±0.56	0.9774	4.740
10	OMK2	4.685±0.59	0.9695	4.542
11	OMK3	4.434±0.55	0.9561	4.239
12	OMK4	4.21±0.51	0.9685	4.077

Wall thickness, release rate constant and permeability coefficient of microspheres prepared by emulsion ionic gelation technique.

The provided table presents the wall thickness, release rate constant, and permeability coefficient of microspheres prepared using the emulsion ionic gelation technique. Let's analyze the data:

Wall Thickness (µ): This parameter indicates the thickness of the wall surrounding the microspheres. It plays a crucial role in controlling the release rate and stability of the encapsulated drug. In this table, the wall thickness ranges from 4.04 µ to 6.12 µ.

Release Rate Constant (mg/hr): The release rate constant represents the rate at which the drug is released from the microspheres over time. It is influenced by factors such as the polymer characteristics, drug-polymer interactions, and microsphere morphology. The release rate constants in this table vary from 0.984 mg/hr to 0.993 mg/hr.

Permeability Coefficient: The permeability coefficient indicates the ability of the drug to permeate through the microsphere wall. A higher permeability coefficient suggests faster drug release. The values provided range from 4.0077 to 6.0796.

Analyzing these parameters provides insights into the performance and characteristics of the microsphere formulations. Differences observed among the formulations may be attributed to variations in formulation components, processing

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techniques, and experimental conditions. Optimal values of these parameters are essential for achieving the desired drug release profile and therapeutic efficacy of the microspheres.

Understanding the relationship between wall thickness, release rate constant, and permeability coefficient is crucial for designing microsphere formulations with tailored drug release kinetics and enhanced therapeutic outcomes. Adjustments in formulation parameters can be made based on these data to optimize the performance of the microspheres for specific drug delivery applications.

Table 6: Wall thickness, release rate constant and permeability coefficient by emulsion ionic gelation technique.

Sl. No	Formulation code	Wall Thickness (μ)	Release Rate Constant (mg/hr)	Permeability Coefficient
1	EMG1	6.12±0.41	0.993	6.0796
2	EMG2	5.63±0.46	0.990	5.5737
3	EMG3	4.63±0.51	0.992	4.5962
4	EMG4	4.04±0.4	0.992	4.0077
5	EMX1	5.85±0.56	0.989	5.7909
6	EMX2	5.68±0.51	0.990	5.6277
7	EMX3	4.85±0.46	0.990	4.8039
8	EMX4	4.44±0.50	0.990	4.3956
9	EMK1	5.12±0.41	0.993	5.0852
10	EMK2	5.25±0.48	0.987	5.1833
11	EMK3	4.65±0.51	0.987	4.5914
12	EMK4	4.43±0.48	0.984	4.3609

IV. CONCLUSION

This study successfully developed and evaluated gliclazide-loaded microspheres using two distinct techniques: Ionic Orifice Gelation and Emulsification Ionic Gelation. The inclusion of various natural gums as mucoadhesive polymers in combination with sodium alginate demonstrated significant effects on the physical and release properties of the microspheres. Key findings include:

Morphology and Physical Properties: Microspheres prepared by Ionic Orifice Gelation exhibited more uniform, spherical morphology, and superior physical properties compared to those produced by Emulsification Ionic Gelation. This method yielded better flowability and compressibility, which are crucial for practical pharmaceutical applications.

Drug Encapsulation and Release: The encapsulation efficiency and drug content varied depending on the formulation parameters. In vitro release studies indicated that both methods could sustain drug release over an extended period, essential for controlled drug delivery systems. However, the Ionic Orifice Gelation technique provided more consistent and controlled release profiles.

Interaction Studies: FT-IR and XRD analyses confirmed significant interactions between gliclazide and the excipients, affecting the drug's crystallinity and dissolution behavior. These interactions are vital for understanding the stability and release mechanism of the drug from the microspheres.

Overall, the Ionic Orifice Gelation technique proved to be superior in producing gliclazide-loaded microspheres with desirable physical attributes and controlled release characteristics. This method holds promise for developing effective controlled drug delivery systems for gliclazide, potentially enhancing patient compliance and therapeutic outcomes in managing diabetes mellitus. Future research could explore the scalability of this method and its applicability to other drugs requiring controlled release.

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