RESEARCH ARTICLE

Impact of Particle Size of Acyclovir Loaded Mucoadhesive Microcapsules on Drug Release Characteristics

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ABSTRACT

This study focuses on the preparation and evaluation of prolonged-release acyclovir (ACV)-loaded mucoadhesive microcapsules using the emulsion solvent evaporation technique with sodium CMC as a mucoadhesive and rate-retarding polymer. The microcapsules exhibited a high yield (92.67–97.85%), drug entrapment efficiency (72.79–92.17%), and mucoadhesion (62–73%). Particle size ranged between 250 µm (F1) and 302 µm (F4), increasing with polymer concentration. In vitro drug release studies conducted in pH 1.2 phosphate buffer revealed an inverse relationship between polymer concentration and release rate. Smaller microcapsules (F1) demonstrated faster drug release (95% in 12 hours), while larger microcapsules (F4) showed sustained release (55% in 12 hours). These insights underscore the importance of optimizing particle size to achieve desired therapeutic outcomes. This study provides valuable data for the development of tailored microcapsule formulations, improving the efficacy and compliance of ACV therapy.

Keywords: Acyclovir, microcapsules, particle size, drug release, mucoadhesion

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INTRODUCTION

Microencapsulation has become a widely adopted approach in drug delivery, offering controlled release and targeted therapy. An innovative oral controlled drug delivery system aims to enhance drug bioavailability and achieve predictable therapeutic outcomes.[1] Oral delivery systems are highly preferred due to their ease of administration and patient compliance. These formulations rely on the gastrointestinal tract (GIT) to absorb the active pharmaceutical ingredient after ingestion.[2] However, a significant limitation of conventional oral administration is the short retention time within the GIT, particularly at primary absorption sites such as the stomach or upper intestine. This may result in insufficient drug release and reduced efficacy of the dose.[3] To address this challenge, confining the drug delivery system to specific regions of the GIT through mucoadhesion is essential. By prolonging the contact time between the drug-loaded polymer and the mucosal surface, mucoadhesive systems improve drug absorption and stability, especially for drugs with limited absorption windows or stability concerns.[4] Mucoadhesion refers to the ability of a material to adhere to the mucosal surfaces of the body, such as those lining the gastrointestinal, nasal, buccal, or vaginal tracts. Classical examples of mucoadhesive polymers include chitosan, alginate, Carbopol, polyvinyl alcohol, HPMC and CMC. These materials are widely used in formulations like buccal tablets, vaginal gels, and nasal sprays for localized or systemic drug delivery. Sodium carboxymethyl cellulose (sodium CMC) is a versatile mucoadhesive polymer widely used in various drug delivery systems due to its ability to interact with mucosal tissues through hydrogen bonding and electrostatic interactions. Its high-water solubility and swelling properties enable it to form a viscous gel upon contact with moisture, enhancing adhesion to mucosal surfaces and prolonging the retention time of drug formulations. It is also employed in controlled-release formulations like microcapsules, where it acts as a rate-retarding agent, and in topical applications, ensuring drug localization and prolonged action. This makes sodium CMC invaluable for improving therapeutic outcomes across diverse drug delivery platforms. Mucoadhesive microcapsules play a pivotal role in drug delivery systems by enhancing the bioavailability and efficacy of therapeutic agents. These microcapsules are designed to adhere to mucosal surfaces, such as those in the gastrointestinal, nasal, buccal, or vaginal areas, through interactions with mucins or epithelial tissues.[5] This adhesion prolongs the residence time of the drug at the absorption site, allowing for sustained and controlled release of the active pharmaceutical ingredient. Additionally, mucoadhesive systems can bypass first-pass metabolism and protect drugs from enzymatic degradation, particularly for peptides, proteins, and other sensitive molecules.[6] By improving drug retention and absorption at targeted sites, mucoadhesive microcapsules are ideal for delivering drugs with poor solubility or short half-lives, ultimately optimizing therapeutic outcomes.[7] Acyclovir (ACV), a synthetic purine nucleoside analogue, is a widely used antiviral medication for managing herpes simplex virus (HSV-1, HSV-2) infections, varicella-zoster, chickenpox, and genital herpes.[8] Despite its therapeutic significance, ACV is categorized as a BCS Class III drug under the Biopharmaceutical Classification System,

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Table 1: Formulation of ACV loaded polymeric Microspheres.

Sr. No	Formulations	ACV (mg)	Na CMC (mg)	Ethanol (ml)	LP (ml)	Span 80 (ml)
1	F1 (1:1)	200	200	50	49	1
2	F2 (1:2)	200	400	50	49	1
3	F3 (1:3)	200	600	50	49	1
4	F4 (1:4)	200	800	50	49	1

Table 2: % yield of ACV loaded microcapsules.

Sr. No.	Formulation	% Yield
1	F1	92.67±1.5
2	F2	94.80±1.3
3	F3	96.21±1
4	F4	97.85±2.1

SD was calculated considering 3 readings

Table 3: DEE of ACV loaded microcapsules.

Sr. No.	Formulations	% EE
1	F1	72.79±1.8
2	F2	83.42±1.9
3	F3	87.28±2.5
4	F4	92.17±1.3

SD was calculated considering 3 readings

indicating high solubility but low intestinal permeability.[9] This characteristic contributes to its low oral bioavailability, with only about 20% of the administered dose being absorbed. Most of its absorption occurs in the upper gastrointestinal tract (GIT), where its solubility is optimal at a pH of 7.0. However, ACV has a short elimination half-life of 2–3 hours, necessitating frequent dosing to maintain therapeutic drug levels, which can lead to patient non-compliance and increased risk of side effects.[10] To overcome these limitations, the development of mucoadhesive prolonged-release microcapsules for ACV is a strategic approach. These microcapsules can adhere to mucosal surfaces in the GIT, prolonging the drug's residence time at its primary absorption sites and enhancing its permeability and absorption.[1] This mucoadhesion facilitates sustained drug release, ensuring consistent therapeutic levels over extended periods while reducing dosing frequency. Furthermore, the controlled release mechanism minimizes fluctuations in plasma drug concentrations, enhancing therapeutic efficacy and reducing systemic side effects. By improving drug targeting, especially in regions with optimal absorption conditions, mucoadhesive microcapsules address both the permeability and bioavailability challenges of ACV, making them an effective solution for optimized antiviral therapy.[6,7] Particle size plays a critical role in the development of prolonged-release microcapsules, directly influencing their drug release behavior, mucoadhesive properties, and overall therapeutic efficacy. Smaller particles have a larger surface area-to-volume ratio, enabling more efficient drug release and better interaction with the mucosal surface, enhancing mucoadhesion.[11] Conversely, larger particles may offer slower drug release, which is beneficial for achieving sustained therapeutic effects over an extended period. The particle size also affects the uniformity of drug dispersion within the microcapsules, ensuring consistent dosing and minimizing variability in drug delivery.[12] Additionally, optimal particle size is crucial for maintaining stability during formulation and ensuring compatibility with the intended route of administration. By carefully controlling the particle size, prolonged-release microcapsules can be tailored to balance sustained drug release, improved bioavailability, and targeted delivery, making it a key parameter in their successful development.[13] This study introduces a novel approach to developing prolonged-release ACV-loaded mucoadhesive microcapsules using the emulsion solvent evaporation technique and sodium CMC as a dual-function polymer for mucoadhesion and rate control. The work stands out by demonstrating a

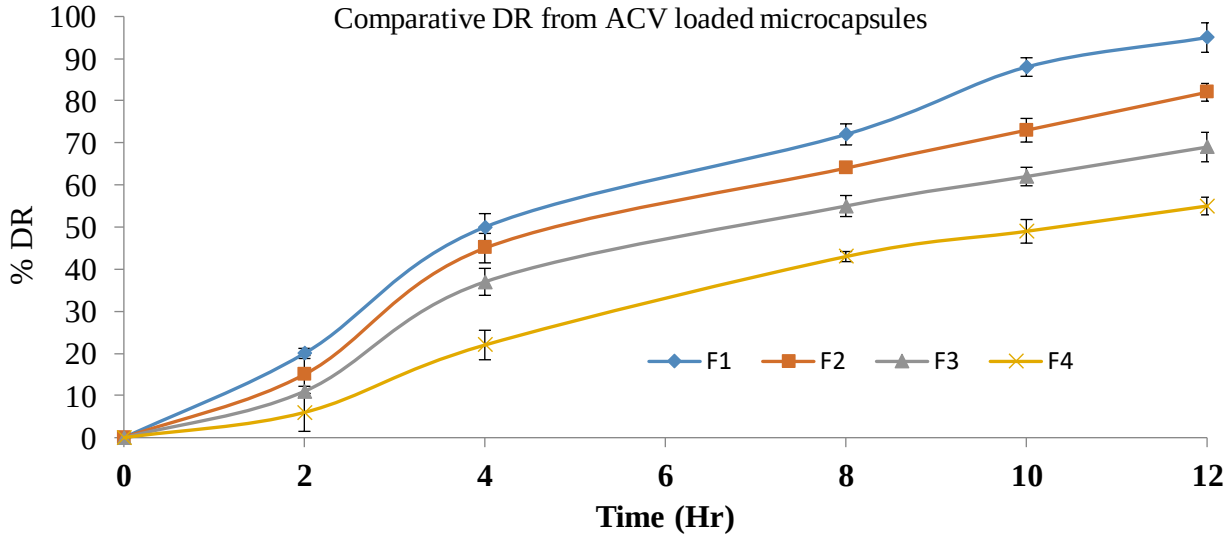

Figure 1: Comparative release of microcapsules in pH 1.2 phosphate buffer.

Table 4: Mucoadhesion of ACV loaded microcapsules.

Sr. No.	Formulations	% Mucoadhesion
1	F1	62±1.3
2	F2	66±1.2
3	F3	69±1.5
4	F4	73±1.1

SD was calculated considering 3 readings

Table 5: DEE of ACV loaded microcapsules.

Sr. No.	Formulations	Particle size (µm)
1	F1	250±2.8
2	F2	265±2.5
3	F3	280±3.1
4	F4	302±3.5

SD was calculated considering 3 readings

systematic correlation between polymer concentration, particle size, offering precise control over therapeutic outcomes. The findings highlight the ability to achieve tailored release profiles, with smaller microcapsules providing rapid drug release and larger ones enabling sustained release, optimizing ACV delivery for various clinical needs. This research advances the design of mucoadhesive systems, improving drug efficacy, patient compliance, and the potential for personalized therapy in managing conditions requiring prolonged ACV administration.

MATERIALS AND METHODS

Materials

Acyclovir (ACV) was obtained as a gift sample from Alpha drug Lab, Indore. Sodium Carboxy Methyl Cellulose (NaCMC) was purchased from Sigma Aldrich, Mumbai. Ethanol, liquid paraffin (LP), Span 80 and n-hexane were purchased from Loba Chemie, Mumbai.

Methods

Development of ACV loaded microcapsules

The emulsion solvent evaporation technique was employed to develop ACV loaded polymeric microcapsules. NaCMC was weighed accurately and added in 50 ml ethanol under continuous stirring to form homogeneous mixture. Batch quantity of ACV was added to this polymeric solution under stirring to form uniform dispersion of drug and polymer. Liquid paraffin (50 ml) was measured in another beaker and span 80 (1 ml) was added to under stirring to mix it properly. This drug-polymer dispersion was poured with syringe and drop wise addition was done in to liquid parrafin solution containing Span 80 under continuous stirring. This emulsion was heated at 80 °C and continuous stirring at 2000 RPM was done for 3-4 hours. Subsequently, n-hexane was added during stirring to harden the microcapsules. The filtration was performed to separate out dried microcapsules using Whatman filter paper. Final drying was performed in a desiccator for 24 hours.[14] Various formulation batches are presented in Table 1 with drug and polymer ratio.

Evaluation of ACV loaded microcapsules

Percentage Yield

The % yield of formulated microcapsules was determined by using following formula[15]

$$\% \text{ Yield} = \frac{\text{Wt of microcapsules}}{\text{Wt.of drug}} + \text{Wt of Polymer X } 100 \quad \ldots(1)$$

Drug entrapment efficiency (DEE)

The microcapsules were first crushed into a fine powder using a mortar and pestle. A precisely weighed 20 mg sample of the powdered microcapsules was suspended in 30 mL of pH 1.2 HCl buffer and sonicated for 30 minutes to facilitate the complete solubilisation and extraction of ACV. The suspension was then filtered to remove undissolved particles, and the filtrate was diluted to 100 mL using the same buffer. The concentration of ACV in the diluted filtrate was quantified using a UV-Visible spectrophotometer.[16] DEE was calculated using below formula.

$$\% \text{ Encapsulation efficiency} = \frac{\text{Actual Drug}}{\text{Theoratical Drug}} \text{ X } 100 \ldots (2)$$

Mucoadhesion testing

The mucoadhesive capacity of the ACV-loaded mucoadhesive microcapsules was evaluated using the *in vitro* wash-off test. Freshly excised sheep stomach mucosa samples (4 × 5 cm) were mounted onto glass slides (3 × 1 inch) using poly cyanoacrylate glue to ensure stability. The tissue was carefully prepared and positioned between two glass slides, forming a suitable surface for testing. The prepared mucosal sample was then attached to the arm of a USP dissolution test apparatus and immersed in a 1000 mL tank containing 900 mL of pH 1.2 buffer, simulating gastric conditions. The test apparatus was operated to move the mucosal sample gently in an up-and-down motion at a constant temperature of 37 °C. The number of microcapsules adhering to the mucosal surface was recorded after 1 hour and subsequently at hourly intervals for up to 12 hours. The percentage mucoadhesion was calculated using below formula.[17]

% Mucoadhesion = (No. of Microcapsules adhered / No. of Microcapsules applied) × 100. ……(3)

Particle size

The average particle size of the ACV loaded mucoadhesive microcapsules was determined using optical microscopy. A small quantity of microcapsules was dispersed onto a glass slide and floated in liquid paraffin to create a stable medium for observation. The prepared slide was placed on the stage of a mechanical microscope. A total of 100 microcapsules were randomly selected and measured for their size using a stage micrometer calibrated for accuracy. The diameter or longest dimension of each microcapsule was recorded, and the measurements were summed to calculate the average particle size.[18]

Drug release study

Study was done in USP type I apparatus (Labindia DS 8000) with pH 1.2 phosphate buffer (900 ml)at 100 RPM and at temp was maintained at 37 ± 0.5°C. An amount of microcapsules equivalent to 200 mg of acyclovir was weighed and added to a dissolution flask containing the buffer solution. The samples (3 ml) were withdrawn at specific time intervals and same quantity of fresh buffer was added each time to maintain the sink condition. The sampling was done at known time points and analysed at 254 nm using UV spectroscopy. The drug release was calculated based on absorbance.[19]

Table 6: Comparative analysis of particle size and DR

Sr. No.	Formulations	Particle size (µm)	% DR at 12 hrs
1	F1	250±2.8	95±3.2
2	F2	265±2.5	82±2.5
3	F3	280±3.1	69±3.5
4	F4	302±3.5	55±3.3

SD was calculated considering 3 readings

RESULTS AND DISCUSSION

Percentage yield

The yield of the microcapsules was determined and it was found between 92.67 to 97.85% as shown in Table 2. The percentage yield of the acyclovir-loaded mucoadhesive microcapsules increased progressively with the increase in polymer concentration from formulation F1 (1:1 drug-to-polymer ratio) to F4 (1:4 drug-to-polymer ratio). F1 demonstrated a yield of 92.67%, while F2, F3, and F4 exhibited yields of 94.80%, 96.21%, and 97.85%, respectively. This trend indicates that higher polymer concentrations contributed to improved microcapsule formation and reduced material loss during the encapsulation process. The increased yield at higher polymer concentrations can be attributed to enhanced entrapment efficiency and stabilization of the microcapsules, as the polymer forms a more robust matrix capable of encapsulating the drug effectively.[20] Thus, the study highlights that optimizing the drug-to-polymer ratio is crucial for maximizing the yield and efficiency of microcapsule formulations.

Drug encapsulation efficiency (DEE)

The DEE of microcapsules was determined and it was found between 72.79 to 92.17 % as shown in Table 3. The % DEE of the ACV loaded mucoadhesive microcapsules showed a clear increase with the rise in polymer concentration, from F1 (1:1) to F4 (1:4).F1 exhibited an % EE of 72.79%, which increased to 83.42% in F2, 87.28% in F3, and 92.17% in F4. This trend suggests that increasing the polymer concentration enhances the encapsulation capacity of the microcapsules, likely due to the formation of a more stable and cohesive polymer matrix that better retains the drug.[21] The higher polymer content reduces the loss of the drug during the encapsulation process, leading to improved entrapment efficiency. As the polymer concentration increases, the viscosity and stability of the formulation improve, enabling better drug retention within the microcapsules, which is essential for achieving prolonged drug release and effective therapeutic outcomes.[22] Thus, the increase in % EE across the formulations indicates the importance of optimizing the drug-to-polymer ratio to enhance both the stability and efficacy of the microcapsules.

Mucoadhesion testing

The % mucoadhesion of microcapsules was determined and it was found between 62 to 73 % as shown in Table 4. The % mucoadhesion of the ACV loaded mucoadhesive microcapsules showed a consistent increase with the rise in polymer concentration from F1 (1:1) to F4 (1:4). Formulation F1 demonstrated 62% mucoadhesion, which increased to 66% in F2, 69% in F3, and reached 73% in F4. This progressive enhancement in mucoadhesion can be attributed to the higher polymer content in the formulations, which increases the availability of functional groups responsible for adhesion to mucosal surfaces. As the polymer concentration increases, the interaction between the microcapsules and the mucosal surface strengthens, resulting in improved retention time at the target site.[23] This enhanced mucoadhesion ensures prolonged contact with the absorption site, facilitating better drug delivery and sustained release. The data underscores the importance of optimizing the drug-to-polymer ratio to maximize mucoadhesion and improve the therapeutic efficacy of the microcapsules.

Particle size of microcapsules

The particle size of microcapsules was determined and it was found between 250 to 302 µm as shown in Table 5. The particle size of the ACV loaded mucoadhesive microcapsules increased progressively with the rise in polymer concentration from F1 (1:1) to F4 (1:4). Formulation F1 exhibited a particle size of 250 µm, which gradually increased to 265 µm in F2, 280 µm in F3, and 302 µm in F4. This trend can be attributed to the higher polymer content in the formulations, which leads to the formation of larger microcapsules due to increased viscosity and more robust polymer matrix formation during encapsulation. Larger particle sizes at higher polymer concentrations can also improve the structural integrity of the microcapsules, contributing to enhanced drug loading and prolonged release. However, the increase in particle size must be balanced with considerations of mucoadhesion and drug release kinetics to ensure optimal performance of the microcapsules.[21,22] Studies, such as those on polyacrylate and alginate microcapsules, confirm that increased polymer content strengthens mechanical properties, resulting in controlled and prolonged drug release. This ensures sustained therapeutic effects by slowing drug diffusion. Additionally, the enhanced wall structure accommodates greater drug loads, protecting them from environmental degradation and optimizing delivery efficiency.[23]

These observations highlight the direct impact of drug-to-polymer ratio on the physical properties of the microcapsules, emphasizing the need for careful optimization in formulation development.

Drug release

The Figure1 shows % drug release as a function of time at interval for batch F1to F4. The *in vitro* drug release data for ACV loaded microcapsules in pH 1.2 phosphate buffer showed a clear inverse relationship between polymer concentration and the rate of drug release. Formulation F1, with the lowest drug-to-polymer ratio (1:1), exhibited the fastest release profile, achieving 95% drug release within 12 hours. As the polymer concentration increased, the drug release rate slowed, with F2 (1:2) releasing 82%, F3 (1:3) releasing 69%, and F4 (1:4) releasing only 55% over the same duration. This trend can be attributed to the higher polymer content in formulations F2 to F4, which forms a denser matrix, thereby prolonging the drug diffusion pathway and reducing the rate of release. The slower release observed in higher polymer formulations

(F3 and F4) aligns with the goal of sustained drug delivery, ensuring prolonged therapeutic effects and reduced dosing frequency. However, the faster release in F1 and F2 may be beneficial for achieving an immediate therapeutic effect. These results highlight the importance of optimizing polymer concentration to balance immediate and sustained release based on therapeutic requirements.

Impact of particle size of microcapsules on release behaviour of ACV

The comparative analysis of particle size of microcapsules and drug release in pH 1.2 phosphate buffers is presented in Table 6. The data indicates a clear relationship between particle size and the drug release (% DR) of ACV from the microcapsules in pH 1.2 phosphate buffer. As the particle size increased from 250 µm in F1 to 302 µm in F4, the drug release over 12 hours decreased significantly, from 95% in F1 to 55% in F4. This inverse relationship can be attributed to the larger particle size of F4, which creates a longer diffusion pathway for the drug to exit the microcapsule matrix, resulting in slower and more sustained release. Conversely, the smaller particle size in F1 provides a larger surface area and shorter diffusion pathways, facilitating faster drug release. This trend is consistent with the influence of polymer concentration, as higher polymer content in formulations like F3 and F4 also contributes to increased particle size and denser matrices, further restricting drug diffusion. The findings highlight the critical role of particle size in modulating the release kinetics of acyclovir, with smaller particles favoring rapid release and larger particles enabling prolonged and controlled drug delivery. These insights are essential for tailoring microcapsule formulations to meet specific therapeutic objectives.

CONCLUSION

The present investigation demonstrates that the particle size of acyclovir (ACV)-loaded mucoadhesive microcapsules significantly influences their drug release characteristics, highlighting its critical role in the development of prolonged-release formulations. Prolonged-release ACV microcapsules were successfully prepared using the emulsion solvent evaporation technique with sodium CMC as the mucoadhesive and rate-retarding polymer. Particle size analysis revealed an increase in size from 250 µmto 302 µm as polymer concentration increased. Drug release studies in pH 1.2 phosphate buffer established an inverse relationship between particle size and release rate, with smaller microcapsules showing faster release and larger ones exhibiting slower sustained release. This relationship is attributed to the longer diffusion pathways and denser matrices in larger microcapsules, which retard drug release. These findings emphasize the importance of optimizing particle size to achieve desired release kinetics and therapeutic outcomes, offering valuable insights for the design of tailored mucoadhesive microcapsule formulations.

REFERENCES

1. Khandbahale SV. Microencapsulation-A novel approach in drug delivery: A review. Asian Journal of Research in Pharmaceutical Science. 2020;10(1):39-50.
2. Baryakova TH, Pogostin BH, Langer R, McHugh KJ. Overcoming barriers to patient adherence: the case for developing innovative drug delivery systems. Nature Reviews Drug Discovery. 2023 May;22(5):387-409.
3. Hua S. Advances in oral drug delivery for regional targeting in the gastrointestinal tract-influence of physiological, pathophysiological and pharmaceutical factors. Frontiers in pharmacology. 2020 Apr 28;11:524.
4. Kumar R, Islam T, Nurunnabi M. Mucoadhesive carriers for oral drug delivery. Journal of Controlled Release. 2022 Nov 1;351:504-59.
5. Komati S, Swain S, Rao ME, Jena BR, Dasi V. Mucoadhesive multiparticulate drug delivery systems: An extensive review of patents. Advanced pharmaceutical bulletin. 2019 Oct;9(4):521.
6. Lopes CM, Bettencourt C, Rossi A, Buttini F, Barata P. Overview on gastroretentive drug delivery systems for improving drug bioavailability. International journal of pharmaceutics. 2016 Aug 20;510(1):144-58.
7. Mansuri S, Kesharwani P, Jain K, Tekade RK, Jain NK. Mucoadhesion: A promising approach in drug delivery system. Reactive and functional polymers. 2016 Mar 1;100:151-72.
8. Andrei G, Snoeck R. Advances and perspectives in the management of varicella-zoster virus infections. Molecules. 2021 Feb 20;26(4):1132.
9. Vaithianathan S, Haidar SH, Zhang X, Jiang W, Avon C, Dowling TC, Shao C, Kane M, Hoag SW, Flasar MH, Ting TY. Effect of common excipients on the oral drug absorption of biopharmaceutics classification system class 3 drugs cimetidine and acyclovir. Journal of pharmaceutical sciences. 2016 Feb 1;105(2):996-1005.
10. Ates M, Kaynak MS, Sahin S. Effect of permeability enhancers on paracellular permeability of acyclovir. Journal of Pharmacy and Pharmacology. 2016 Jun;68(6):781-90.
11. Lengyel M, Kállai-Szabó N, Antal V, Laki AJ, Antal I. Microparticles, microspheres, and microcapsules for advanced drug delivery. Scientia Pharmaceutica. 2019;87(3):20.
12. Jantzen GM, Robinson JR. Sustained-and controlled-release drug delivery systems. Drugs and The Pharmaceutical Sciences. 2002;121:501-28.
13. Yoo JW, Doshi N, Mitragotri S. Adaptive micro and nanoparticles: temporal control over carrier properties to facilitate drug delivery. Advanced drug delivery reviews. 2011 Nov 1;63(14-15):1247-56.
14. Tao Y, Lu Y, Sun Y, Gu B, Lu W, Pan J. Development of mucoadhesive microspheres of acyclovir with enhanced bioavailability. International journal of pharmaceutics. 2009 Aug 13;378(1-2):30-6.
15. Shivhare UD, Chhabra GS, Mathur VB, Patel SB. Microencapsulation of acyclovir into Eudragit S100 using emulsion-solvent evaporation method. Research Journal of Pharmacy and Technology. 2011;4(4):652-8.

16. Ben ES, Nofita R, Rusdi S, Suardi M, Djamaan A. Use of eudragit RS PO in the formulation of acyclovir hollow-microspheres by solvent evaporation technique. Der Pharm Lett. 2016;8(11):53-9.
17. Amin ML, Ahmed T, Mannan MA. Development of floating-mucoadhesive microsphere for site specific release of metronidazole. Advanced pharmaceutical bulletin. 2016 Jun;6(2):195.
18. Sriram N, Katakam P. Formulation and evaluation of mucoadhesive microspheres of pioglitazone hydrochloride prepared by ionotropic external gelation technique. Journal of Encapsulation and Adsorption sciences. 2016 Mar 2;6(1):22-34.
19. Bashir Khan A, Sharnagat Thakur R. Formulation and evaluation of mucoadhesive microspheres of tenofovir disoproxil fumarate for intravaginal use. Current drug delivery. 2014 Feb 1;11(1):112-22.
20. Jyothi NV, Prasanna PM, Sakarkar SN, Prabha KS, Ramaiah PS, Srawan GY. Microencapsulation techniques, factors influencing encapsulation efficiency. Journal of microencapsulation. 2010 May 1;27(3):187-97.
21. Lee H, Choi CH, Abbaspourrad A, Wesner C, Caggioni M, Zhu T, Weitz DA. Encapsulation and enhanced retention of fragrance in polymer microcapsules. ACS applied materials & interfaces. 2016 Feb 17;8(6):4007-13.
22. Wong CY, Al-Salami H, Dass CR. Microparticles, microcapsules and microspheres: A review of recent developments and prospects for oral delivery of insulin. International journal of pharmaceutics. 2018 Feb 15;537(1-2):223-44.
23. Wu Y, Zhang W, Huang J, Luo Z, Li J, Wang L, Di L. Mucoadhesive improvement of alginate microspheres as potential gastroretentive delivery carrier by blending with Bletilla striata polysaccharide. International journal of biological macromolecules. 2020 Aug 1;156:1191-201