INFLUENCE OF ETHYL CELLULOSE CONCENTRATION ON THE RHEOLOGICAL BEHAVIOR AND STABILITY OF EC/PVA MICROSPONGES FOR DRUG DELIVERY APPLICATION

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ABSTRACT

This study investigated the influence of flow behavior on the preparation of microsponges to enhance their stability for drug delivery applications. The viscosity of ethyl cellulose (EC) was modified by varying its concentration)3,4 and 5%wt) to evaluate its effect on the stability of the microsponges. Rheological properties were assessed using a cone-plate viscometer, generating viscosity, flow, and fitting curves to analyze ethyl cellulose behavior and its role in maintaining microsponges' integrity. Zeta potential measurements were conducted to evaluate colloidal stability while scanning electron microscopy (SEM) was used to examine the morphology of microsponges. The results indicated that the microsponge systems followed a power law model, exhibiting non-Newtonian shear-thining behavior, as evidenced by decreased viscosity with increasing shear rate. SEM analysis revealed a microsponge diameter ranging from 9.08 to 30.42 μm. Zeta potential values of (-36,-35, and -35) mV confirmed good stability. Overall, the findings revealed that increasing the viscosity of ethyl cellulose led to a slight decrease in microsponge stability. However, the stability remained within an acceptable range. Notably, the formulation (M1) exhibited the highest stability, with a zeta potential value of −36 mV, indicating superior dispersion stability. Therefore, M1 can be considered the optimum sample based on its balance between viscosity and stability.

Keywords: Microsponge, Rheology, Viscosity, Flow behavior, **Stability .**

INTRODUCTION

Microsponges function as polymeric drug delivery systems which trap pharmaceutical agents to improve delivery performance by enabling lower controlled dosage levels (Jayasawal et al., 2022), (Biharee et al., 2023). The porous structure of these systems allows active agents to release at controlled rates over time which makes them suitable for targeted drug delivery applications (Abass et al., 2021). Microsponges provide stability

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enhancement while they sustain drug concentrations in the body and reduce adverse effects (Srinatha et al., 2024). The size of these systems ranges between 5 to 300 μm with each 25 μm particle containing about 250,000 pores (Wu, 2021). Ethyl cellulose (EC) serves as the primary material for microsponge synthesis because it creates excellent films while maintaining thermal stability and showing broad compatibility with various active pharmaceutical ingredients (Qureshi et al., 2024). The viscosity of ethyl cellulose solutions depends on concentration because it determines both microsponge structure and stability (Hadi et al., 2019). The rheological properties of polymers need thorough understanding during formulation development because they determine both dispersion uniformity and system stability(Rathnam & Sangeetha, 2024). Research indicates that microsponges demonstrate non-Newtonian behavior through shear thinning because their viscosity decreases when subjected to higher shear rates(Hameed & Sabri, 2024) . The drug delivery system benefits from this property because it produces uniform particles which enhances delivery efficiency (Halder et al., 2024). Despite these advantages, limited studies have investigated the direct effect of ethyl cellulose viscosity on the morphological and colloidal stability of microsponges. Therefore, this study aims to fill this gap by investigating how varying ethyl cellulose viscosity affects the formation and stability of microsponges, ultimately contributing to the identification of the optimal formulation for improved performance.

MATHEMATICAL RELATIONS

Ethyl Cellulose (Sigma-Aldrich), Polyvinyl Alcohol (PVA,Mitsui Chemicals), and Dichloromethane (DCM) from (Merck) were utilized as a solven.

Three microsponge samples were fabricated using ethyl cellulose and polyvinyl alcohol (PVA) to enhance moisture retention and biological efficacy. PVA was dissolved at a concentration of 3% in water, while different concentrations of ethyl cellulose (3%, 4%, and 5wt%) were used to prepare the microsponge as shown in table 1. After dissolving EC in DLM, PVA was added with stirring, and mixing continued for 4 h until a homogeneous mixture was obtained. The mixture was then filtered using filter paper for 24 h to separate the formed microsponge. The microsponges were thoroughly examined to confirm their formation using scanning electron microscopy (SEM).

Table1. Formulation Parameters for Microsponge Preparation

Run	EC (%)	PVA (%)	RPM Speed	Microsponges
1	3	3	1000	M1
2	4	3	1000	M2
3	5	3	1000	M3

The viscosity curves and flow curve of samples found by using a cone-plate viscometer according to ASTM D7395(Mohammed et al., 2022). The samples were carefully prepared to be free of impurities, and their viscosity was measured by determining the resistance under various shear forces. Three concentrations of ethyl cellulose. Three measurements were taken for each sample to understand its rheological behavior across multiple

temperatures, aiding in formula optimization. Rheological applications were employed to analyze the viscosity data, where the measurements were input, and suitable rheological models.

For zeta potential determination, 1 ml of the microsponges suspension was placed in a clear disposable zeta cell, assuring that no air bubbles were present in the sample. The system was set to a temperature of 25°C, and an electric field of approximately 15 V/cm was applied. The results were recorded, with a more negative zeta potential indicating greater stability of the microsponge formulation. Each sample was subjected to triplicate testing (n = 3). These measurements were conducted to assess the stability of the microsponges, as presented in Table (2).

Table 2. Zeta potential [mV] values (Ahmadi et al., 2022).

Zeta potential [mV]	Stability behavior
5	Rapid coagulation or flocculation
10-30	Incipient instability
30-40	Moderate stability
40-60	Good stability
More than 61	Excellent stability

Analytical scanning electron microscope (SEM), model (JEOL 6400 F) used to examine the morphology of microsponges according to (ASTM 986-04). The sample was then coated with a 20 nm thick layer of gold using a cathodic evaporator. Images were captured using specialized computer software, and the diameters of individual microsponges were measured from these recorded image.

RESULTS AND DISCUSSION

A rheological study was conducted on EC by analyzing the flow and viscosity curves at different EC concentrations (3, 4 and 5%wt) as shown in Fig.(1). The results indicated that the microsponge follows a power law model, where the viscosity decreases with increasing shear rate, reflecting its non-Newtonian flow (Ferreira et al., 2020). The viscosity measurements showed continuous growth when EC concentration increased thus indicating the development of a cohesive network structure. The maximum EC concentration (M3) led to increased shear stress resistance which caused both an elevated consistency index (k) value and reduced temperature effects on emulsion structure (Ahmadi et al., 2022).

The studied formulations demonstrated non-Newtonian fluid behavior through their shear stress and shear rate relationship which exhibited a gel-like structure. The viscosity curve showed non-Newtonian flow behavior together with shear-thinning characteristics at 3%, 4% and 5% EC concentrations particularly at the higher concentrations. The EC chains align better at elevated shear rates which causes a reduction in flow resistance and a decrease in viscosity (Ahmadi et al., 2022). The shear thinning effect became more intense at elevated concentrations because the EC chains aligned better with increased

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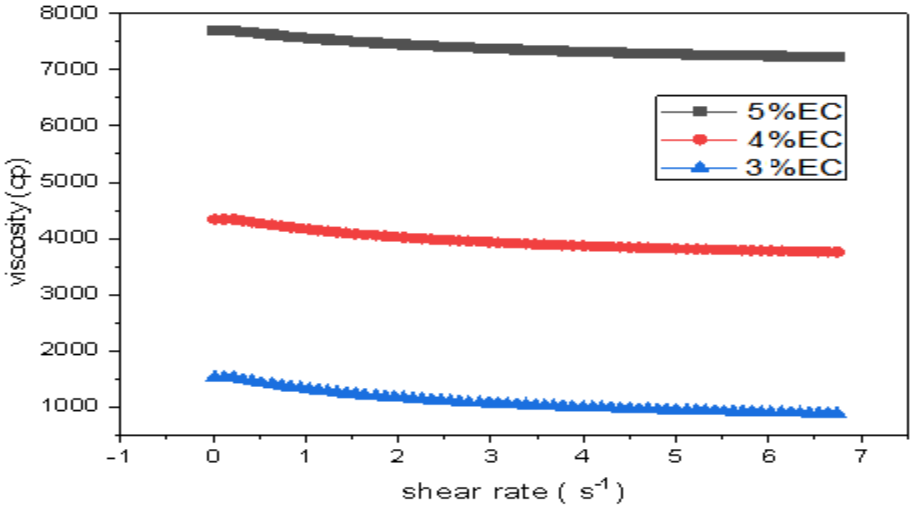

Fig .1. The viscosity vs shear rate for (3,4,5 wt.%) EC.

Fig.2 shows the flow curve for all EC concentrations. In this curve, we observe that as the shear rate increases, the shear stress increases. This behavior demonstrates that the material exhibits a non-Newtonian behavior, whereby increasing shear rate results in an increase in the stress experienced by the fluid (Yan et al., 2022). The reason behind this behavior is that the EC chains become more aligned or organized when the fluid is subjected to high shear forces (Chandurkar et al., 2024) , (Muneer et al., 2021). As the shear rate increases, the molecular chains in the EC begin to orient in directions that align with the fluid movement, reducing flow resistance and increasing the fluid's mobility. This results in an increase in shear stress. At higher EC concentrations (such as 4% and 5%), this effect becomes more pronounced. This is because the EC chains are denser, making them more resilient to shear forces. Consequently, the molecular structure changes to become more flexible, allowing for increased flow at higher shear speeds without collapse or loss of structural stability. This effect essentially reflects the shear-thinning behavior observed in many polymers with long molecules or complex structures, such as EC.

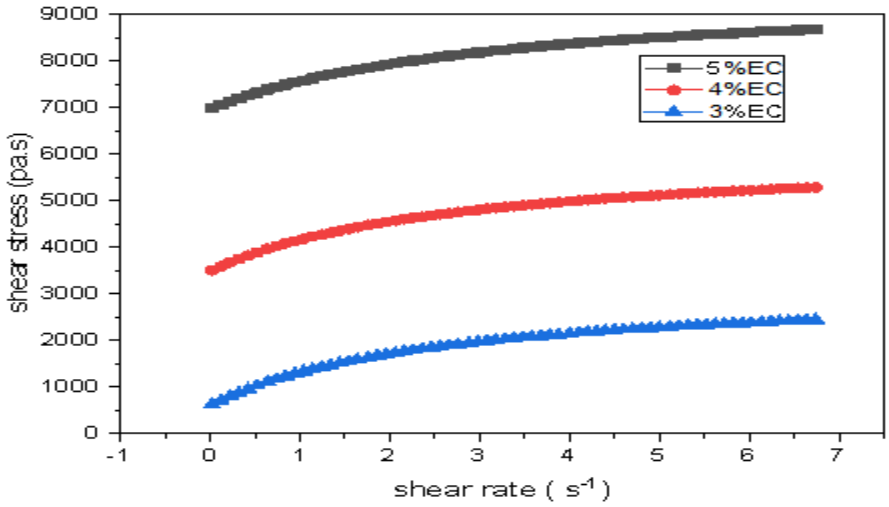

Fig .2. The shear stress vs shear rate for (3,4 and 5 wt.%) EC.

From the (Rheology Lite for Windows) APP, it was found that the optimal model for EC is power law model, as shown in Fig.3. It showed a clear shear-thinning rheological behavior for all formulations, as evidenced by the calculated values of flow index (n), which were all less than 1 (0.769, 0.748, 0.738) as shown in table (3). This reflects a decrease in the system viscosity with increasing shear rate due to the rearrangement of the EC chains due to shear forces. This behavior suggests that the molecular structure of the polymer undergoes dynamic transformations during flow, as the long chains orient and resolve temporary cross-links in the direction of flow, facilitating movement and reducing flow resistance (Ding & Li, 2021) (Assmaa & Hadi, 2025)(Hadi et al., 2025). Furthermore, the steadily increasing consistency constant K, from 474.64 to 549.58 with concentration, shows that the system viscosity at low shear rates becomes higher as the EC content increases, due to the increased number of interaction points between the molecular chains within the carrier medium. The high values of the coefficient of determination ($R^2 > 0.85$) reflect a good fit between the power law model and experimental data, supporting the model's reliance on interpreting the flow behavior of these systems. All of these results

indicate that increasing the polymer concentration enhances the structural stability of the system under shear conditions and increases its ability to maintain its rheological properties over a wide range of shear rates. This is an important indicator for applications that require high performance stability under variable operating conditions.

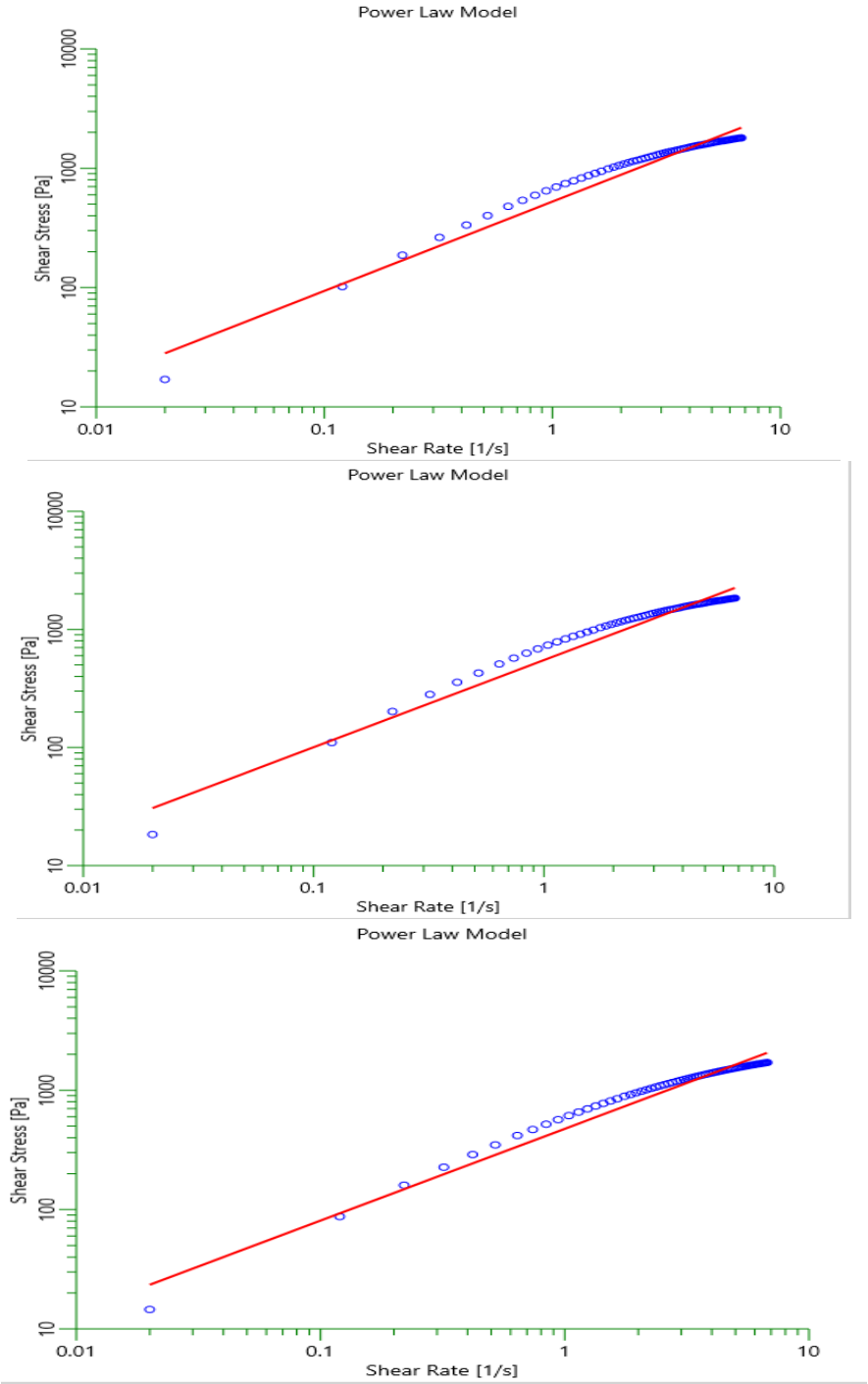

Fig .3. Curve fitting model of EC at 3,4 and 5%wt.

Table 3. Consistency constant K and flow index n of EC at 3,4 and 5%wt.

Power Law Model	K (Pa.s^n)	n	Relative Error (%)	R^2
3%EC	474.64	0.769	15.104	0.892167
4%EC	525.13	0.748	16.325	0.86773
5%EC	549.58	0.738	16.794	0.856275

The scanning electron microscope (SEM) of microsponge showed that the microscopic images revealed that the microsponge was homogeneously formed, with clear and evenly distributed pores[21], indicating a tight and precise manufacturing process as shown in Fig.4. The structural characteristics confirmed the high ability of the microsponge to absorb and evenly distribute active ingredients.

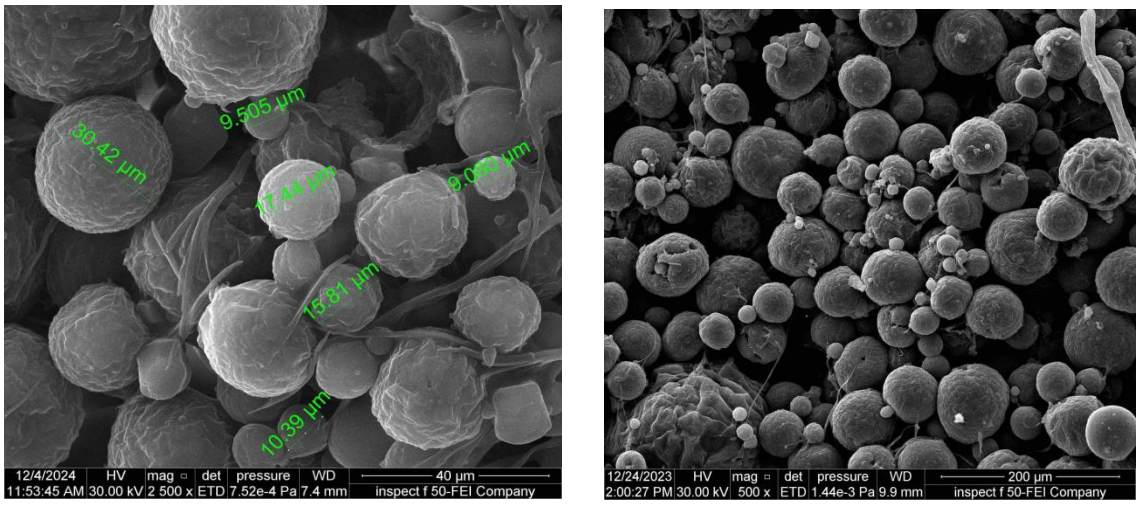

Fig .4. The SEM images of M3

The physical characteristics of the prepared microsponges were evaluated using ethyl cellulose at concentrations of (3,4, and 5wt%), with PVA serving as the emulsifying agent. The average particle diameter was analyzed using scanning electron microscopy (SEM), as well as zeta potential. The results showed in Table (4) that the electrostatic stability of the microsponges was evaluated through zeta potential measurements. Sample M1 showed a value of -36 mV, indicating good stability and the value remained at -36 mV in sample M2. These reflect that the stability and electrostatic repulsion between the microsponges prevent their agglomeration, as the value if greater than 30 - indicates good stability [22]. As for sample M3, it recorded a value of -35 mV, which is normal because ethyl cellulose is a non-ionic polymer, i.e. it does not directly affect the zeta potential, but it may interact with ions in the medium, which affects the zeta potential [23]. This may be due to the formation of particle clusters due to the high concentration of ethyl cellulose. As a result, all samples had good stability based on these results.

Table 4. Zeta Potential (mV) of M1, M2 and M3.

Sample	Zeta potential [mV]
M1	-36
M2	-35
M3	-35

CONCLUSIONS

This study examined how flow behavior affects ethyl cellulose (EC) microsponge preparation for improving the stability of microsponges. The results indicated that the microsponge follows a power law model, where the viscosity decreases with increasing shear rate, reflecting its non-Newtonian flow. When ethyl cellulose concentration increased between 3% and 5% wt, the viscosity increased. Clear shear-thinning rheological behavior for all formulations, as evidenced by the calculated values of n, which were all less than 1 (0.769, 0.748, 0.738). Consistency constant K increasing from 474.64 to 549.58 with concentration, shows that the viscosity at low shear rates and stability becomes higher. Zeta potential measurements confirmed good stability of the microsponges within prepared samples because their values spanned from -35 to -36 mV thus ensuring electrostatic stability which prevented particle aggregation in the system. The Scanning Electron Microscopy (SEM) images showed that the microsponges consisted of uniform particles that had regular shapes and uniform pores that improved their ability to distribute active ingredients homogeneously. The study demonstrates that elevated ethyl cellulose concentrations create less stable microsponges. These systems demonstrate potential use in drug delivery applications. This study establishes a foundation for developing drug delivery systems with high stability and reliable performance by investigating the flow behavior of EC. Also, M1 can be considered the optimum sample based on its balance between viscosity and stability.

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