RESEARCH ARTICLE

Quality by Design Approach to Nasal Mucoadhesive Microspheres: Enhanced Sumatriptan Succinate Delivery through Formulation and Characterization

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ABSTRACT

The primary therapeutic indications for sumatriptan succinate (STS) include the treatment of migraine and cluster headaches. To enhance mucoadhesion, sodium carboxymethyl cellulose (SCMC) and hydroxyl propyl methyl cellulose (HPMC K15M) were used in this study to develop nasal mucoadhesive microspheres of STS. A central composite design, facilitated by Design Expert software, was employed to assess the impact of polymer concentrations on mucoadhesion, involving nine different formulations. The study's findings indicated that the microspheres were uniformly sized and spherical and that the polymers were compatible with STS. The optimal formulation, consisting of 220.711 mg of SCMC and 150 mg of HPMC K15M, demonstrated the highest level of mucoadhesion. This combination effectively regulated the discharge of STS from the mucoadhesive microspheres and significantly improved their mucoadhesive properties. These results suggest that the strategic use of SCMC and HPMC K15M can enhance the performance of nasal mucoadhesive microspheres, ensuring a controlled release of STS and improved adhesion to mucosal surfaces. This has the potential to optimize the therapeutic efficacy of STS in treating migraine and cluster headaches.

Keywords: Drug release, Mucoadhesive microspheres, Sodium carboxymethyl cellulose, Sumatriptan succinate.

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INTRODUCTION

The main indication for the drug sumatriptan succinate (STS) is the treatment of cluster and migraine headaches. It is a member of the triptan drug family, which acts by activating serotonin (5-HT) receptors in the brain, which narrows blood vessels and lowers inflammatory neuropeptides.[1] The effects of STS include the relief of headache, nausea, light and sound sensitivity, and other migraine-related symptoms. Because it comes in a variety of forms—oral tablets, nasal sprays, and subcutaneous injections—administration options may be tailored to the specific needs of the patient and the intensity of their symptoms.[2] Common side effects, albeit usually easily tolerated, might include tiredness, dizziness, and warmth or tingling feelings. STS should be used with caution in individuals with cardiovascular conditions due to its vasoconstrictive properties. Overall, it represents a significant advancement in migraine management, providing rapid and targeted relief for sufferers.[3]

Nasal mucoadhesive microspheres are an innovative drug delivery system designed to enhance the bioavailability and efficacy of medications administered through the nasal route.[4] These tiny, spherical particles adhere to the mucosal lining of the nasal cavity, ensuring prolonged residence time and sustained drug release facilitated by mucoadhesive polymers such as chitosan, alginate, or carbomers.[5] The nasal route offers rapid absorption due to the rich vascularization of the nasal mucosa, avoidance of first-pass metabolism, and non-invasiveness, making it suitable for patients with difficulty swallowing pills. Nasal mucoadhesive microspheres enhance these benefits by protecting the drug from degradation, providing a controlled release profile, and improving patient compliance through reduced dosing frequency.[6] They are

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particularly useful for delivering drugs requiring quick onset of action, such as treatments for migraines, allergies, or hormonal deficiencies, and are being explored for administering vaccines and biologics due to the nasal cavity's potential to stimulate both local and systemic immune responses. Formulation techniques such as spray drying, coacervation, or emulsion-based methods ensure uniform size and high encapsulation efficiency, while characterization assesses their size, surface morphology, mucoadhesive strength, drug loading capacity, and release kinetics to ensure optimal performance.[7] Overall, nasal mucoadhesive microspheres represent a promising approach to drug delivery, offering improved bioavailability, patient convenience, and therapeutic efficacy.

STSmucoadhesive microspheres represent an advanced approach to migraine treatment, leveraging the benefits of both mucoadhesive technology and the efficacy of STS. These microspheres are engineered to adhere to the mucosal lining of the nasal cavity, allowing for extended retention and gradual release of the drug. This delivery method is particularly advantageous for STS, a serotonin (5-HT) receptor agonist, as it provides a rapid onset of action crucial for acute migraine relief while enhancing bioavailability by bypassing the gastrointestinal tract and first-pass metabolism.

The mucoadhesive properties are achieved using polymers such as chitosan, alginate, or carbomers, which form strong interactions with the mucus layer in the nasal cavity. This ensures that the microspheres remain in place, facilitating sustained drug discharge and refining patient acquiescence by slashing the frequency of administration. The nasal route is especially suitable for STS due to the rich vascularization of the nasal mucosa, which allows for quick absorption into the systemic circulation, providing prompt relief from migraine symptoms. Formulation of these mucoadhesive microspheres involves techniques like spray drying, coacervation, or emulsion-based methods, which ensure uniform particle size, high encapsulation efficiency, and stability. Characterization of the microspheres includes evaluating their size, surface morphology, mucoadhesive strength, drug loading capacity, and release kinetics, ensuring that they meet the desired therapeutic outcomes.[8] Overall, STSmucoadhesive microspheres offer a promising and effective solution for migraine management, combining the rapid and targeted relief provided by nasal delivery with the prolonged action afforded by mucoadhesive technology. This innovative approach not only enhances therapeutic efficacy but also improves patient convenience and adherence to treatment regimens.

The present study aimed to develop STS nasal mucoadhesive microspheres using a central composite design facilitated by Design Expert software. Sodium carboxymethyl cellulose (CMC) and hydroxypropyl methylcellulose (HPMC K15M) were the independent variables chosen for their mucoadhesive properties. The percentage of mucoadhesion was the dependent variable, crucial for ensuring prolonged retention and effective drug release in the nasal cavity. By optimizing the levels of these polymers, the study sought to achieve optimal mucoadhesion, enhancing drug absorption and therapeutic efficacy. Design Expert software enabled a systematic and statistical approach, identifying the optimal formulation parameters and leading to the development of an effective nasal delivery system for STS.

MATERIALS AND METHODS

Materials

The source of sumatriptan succinate was Healing Pharmatech Private Limited, Hyderabad, India. Fischer Scientific, India, provided the sodium carboxy methyl cellulose (sod. CMC), and HPMC K15M, Purified water was used where ever required.

Preparation of microspheres

Nasal mucoadhesive microspheres of STS were formulated using the ionotropic gelation method. Sodium carboxymethyl cellulose (SCMC) solutions of varying concentrations were prepared in distilled water and placed in a 250 mL beaker. STS was dissolved in a hydroxypropylmethylcellulose (HPMC) K15M solution. The drug-polymer mixture was then added dropwise to a sodium tripolyphosphate solution using a 22-gauge needle, with continuous rousing at 1000 rpm for 1 hour at room temperature.[9] The resulting microspheres were decanted, rinsed with distilled water, and dried overnight (Table 1).

Compatibility Studies

Fourier Transform Infrared Spectroscopy (FTIR) was utilized to evaluate the compatibility of STS with various excipients. Samples of pure STS and each excipient, including SCMC and HPMC K15M, were accurately weighed. Each sample was then ground with spectroscopic grade KBr powder and compressed into pellets using a hydraulic press under controlled pressure. FTIR spectra for both the pure STS and excipients, as well as for physical mixtures of STS with each excipient, were recorded using an FTIR spectrophotometer. The spectra were analyzed to detect any shifts, new peaks, or changes in characteristic functional groups of STS, which could indicate potential interactions or compatibility issues with the excipients. This analysis aimed to confirm that the selected excipients do not compromise the chemical stability or efficacy of STS in the formulated microspheres.

Particle Size

Counting approximately 100 microspheres using a calibrated optical microscope provides a reliable estimate of the particle size distribution within the sample.[10] This method involves

Table 1: Different inputs and outputs used in the study

Independent variables	*Levels*		
	Low	*Medium*	*High*
X_1= HPMC K15M (mg)	100	150	200
X_2= sodium carboxymethyl cellulose (mg)	100	150	200
Distorted values	-1	0	+1
Responses experiential	*Conditions*		
Y_1= %mucoadhesion	Maximize		

randomly selecting and measuring the diameter of each microsphere visible under the microscope. By averaging these measurements, statistical parameters such as mean diameter and size distribution can be calculated. This approach ensures a representative sampling and accurate characterization of the microspheres' particle size, which is essential for quality control and maintaining consistency in pharmaceutical formulations.[11]

%Yield

After preparing the microspheres, each batch was carefully weighed to determine its final mass. The efficiency of the manufacturing process was assessed by calculating the percentage yield of the microspheres. This was done by dividing the weight of the prepared microspheres by the total weight of all excipients and medications used in their making, including SCMC, HPMC K15M, and STS. The percentage yield provides insight into the effectiveness of the formulation and production process. A higher yield indicates a more efficient process with minimal material loss, while a lower yield may suggest the need for process optimization or troubleshooting.[12]

Entrapment Efficiency (EE)

To quantify the amount of STS in each batch, 100 mg of STS microspheres from each batch were first agitated in 3 mL of 1% w/v sodium citrate solution until fully dissolved. To further solubilize the STS, 7 mL of methanol was then added to the solution. After appropriate dilution, the absorbance of the filtrate at 228 nm was measured using a UV-visible spectrophotometer.[13] This absorbance measurement allows for the determination of the drug concentration in the solution, providing an estimate of the STS content in the microspheres (eq.1).

$$\%EE = \frac{Actual\ MNZ\ loading}{Theoritical\ MNZ\ loading} x\ 100 \text{--- (1)}$$

***Ex vivo* mucoadhesion test**

The falling liquid film method was used to assess the microspheres' in vitro mucoadhesion. A glass slide containing a goat nasal mucosa strip was utilized, and 25 mg of precisely weighted microspheres were dropped onto it. After allowing the microspheres to interact with the mucosa for 15 minutes, the glass slide was positioned at a 45° angle. Phosphate-buffered saline (PBS) at pH 6.4 was then passed over the membrane for five minutes at a flow rate of 1-mL/min, using a burette. The eluate was collected in a watch glass, and the remaining particles on the mucosa were dried and weighed. The study also noted that mucoadhesion was influenced by the surface area of the microspheres, with increased mucoadhesion correlating with a larger particle surface area.[14]

***In-vitro* dissolution**

A modified diffusion cell was used to evaluate the drug release from the microspheres. The release medium consisted of 50 mL of pH 6.4 phosphate buffer solution in a 250 mL beaker. The semi-permeable membrane (cellulose nitrate membrane with a 0.45 µm pore size and 47 mm diameter) was soaked in the buffer for 6 to 8 hours to activate it. Once activated, the semi-permeable membrane was used to suspend a weighed quantity of microspheres containing 20 mg of propranolol HCl in the release medium. The setup was maintained at 37 ± 2ºC with continuous stirring at 50 rpm using a magnetic stirrer. Every hour, 1 mL samples were withdrawn, diluted to 10 mL with pH 6.4 buffer solution, and their absorbance was measured at 290 nm using a double-beam UV spectrophotometer, with the release medium serving as a blank. To maintain the volume of the release medium, 1-mL of buffer was added after each sample withdrawal. This study was conducted over a period of seven hours, allowing for comprehensive monitoring of the drug release profile from the microspheres.[15]

Statistical Analysis

To find statistically significant differences between groups, data from numerous research were analysed using one-way analysis of variance (ANOVA). A statistical significance threshold of $p < 0.05$ was applied to ascertain the results. This threshold ensures that any observed variations are unlikely due to random fluctuations, thereby increasing confidence in the validity and repeatability of the formulation outcomes and experimental results.

RESULTS AND DISCUSSION

Fourier Transform Infrared (FTIR) Studies

The FTIR measurements indicated that there were no interactions between the polymers used in the microsphere formulation and the medication. This conclusion is supported by the absence of any modifications in the fingerprint region of the FTIR spectra of the pure drug, as depicted in Figure 1. The fingerprint region of an FTIR spectrum contains unique absorption patterns that are characteristic of specific functional groups and molecular structures. If significant interactions or chemical changes had occurred between the drug and the polymers, these patterns would have shifted, or new peaks would have appeared in this region.

The consistent fingerprint region spectra of the pure drug, even after incorporating it with the polymers, confirm that there are no notable chemical interactions or alterations in the drug's functional groups. This observation suggests that the drug and polymers used in the microsphere formulation are chemically compatible, which is crucial for ensuring the stability and efficacy of the final product. The absence of chemical interactions reassures that the microspheres will maintain the drug's intended therapeutic properties and performance (Figure 1).

Physicochemical Results of the Formulations

The study assessed various parameters of nine different formulations of STS mucoadhesive microspheres, including particle size, yield, and drug content. The results of these evaluations are summarized in Table 2.

Table 2: Physicochemical assets of prepared mucoadhesive microspheres

Formulation	*Particle size (mm)*	*Yield (%)*	*Drug content (%)*	*Swelling index (%*
F1	1.11 ± 0.03	83.51 ± 2.62	88.25 ± 0.08	60.52 ± 1.75
F2	1.05 ± 0.07	84.72 ± 1.41	89.65 ± 2.09	61.82 ± 1.61
F3	1.08 ± 0.06	81.64 ± 3.95	90.51 ± 3.58	72.94 ± 2.49
F4	1.17 ± 0.04	84.06 ± 2.64	91.32 ± 2.16	69.32 ± 1.85
F5	1.15 ± 0.06	79.52 ± 1.74	91.21 ± 1.78	70.25 ± 3.06
F6	1.19 ± 0.06	89.95 ± 1.06	93.25 ± 4.62	73.07 ± 2.58
F7	1.32 ± 0.02	78.45 ± 1.85	91.65 ± 3.27	66.78 ± 1.28
F8	1.18 ± 0.03	81.09 ± 2.48	89.84 ± 1.48	69.11 ± 3.16
F9	1.24 ± 0.01	77.84 ± 3.13	85.65 ± 5.26	70.51 ± 2.36

Values in mean ± SD; n = 3

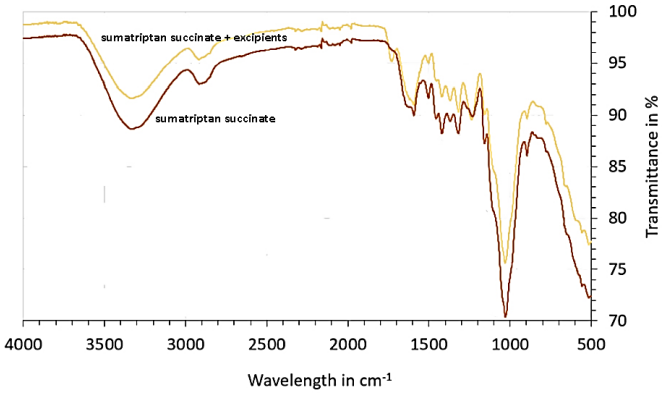

Figure 1: FTIR spectrum of pure STS and with the excipients

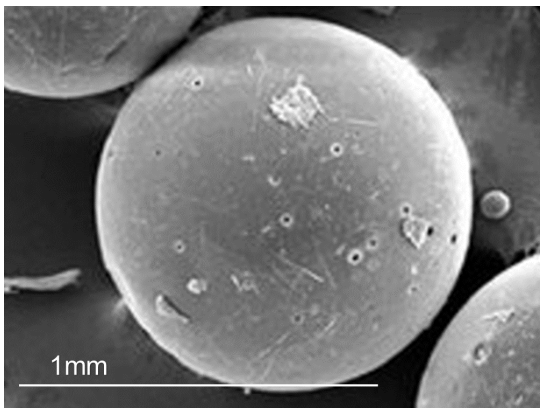

Figure 2: Surface morphology imagined with SEM

The particle size of the microspheres varied from 1.05 ± 0.07 to 1.32 ± 0.02 mm, with formulation F3 having the smallest particle size and formulation F7 the largest. This variation is due to the differing polymer concentrations in each formulation. Smaller particles generally provide enhanced drug release rates because of their increased surface area, which is important for achieving effective therapeutic outcomes. The yield of the formulations ranged from 77.84 ± 3.13 to 89.95 ± 1.06%. F6 containing 220.711 mg of SCMC and 150 mg of HPMC K15M showed a good %yield. All the formulations exhibited relatively high yields (above 75%), indicating efficient production processes. Drug content varied from 85.65 ± 5.26 to 93.25 ± 4.62%, with Formulation F6 having the highest drug content and Formulation F7 following closely at 91.65 ± 3.27%. High drug content reflects efficient encapsulation and minimal drug loss during the microsphere formation. However, Formulation F9, with the lowest drug content, indicates potential inefficiencies in the encapsulation process or stability issues.[16-22]

The results indicate that the choice and concentration of polymers have a significant impact on the properties of STS mucoadhesive microspheres. Formulations F6 emerged as the most promising candidates due to their favorable characteristics. Formulation F2, with its smaller particle size, may facilitate more efficient drug release, while Formulation F6, with its high drug content, demonstrates effective encapsulation. In contrast, Formulation F9 exhibited the poorest performance regarding yield and drug content, suggesting that its formulation parameters need optimization. Improvements could involve adjusting polymer concentrations or modifying the preparation process to enhance encapsulation efficiency and yield. Overall, the study underscores the importance of optimizing formulation parameters to achieve the desired microsphere characteristics. The findings suggest that Formulation F6 shows significant potential for effective controlled drug release and mucoadhesion of STS, making them suitable candidates for further in vivo studies and potential clinical applications.[23-29]

Scanning Electron Microscopy (SEM) Study

SEM images of the microspheres revealed their spherical, distinct, and free-flowing nature, reflecting the consistency and quality of the microsphere manufacturing process. The morphological evaluation also highlighted the porous surfaces of the microspheres, which are crucial as they indicate potential pathways for drug release. These pores were observed to increase in size and number as the drug dissolved, suggesting a mechanism by which the drug gradually permeates through these channels. The progressive enlargement of the pores over time implies a controlled release profile, allowing for continuous drug delivery. This porous structure enhances

the effectiveness and safety of the drug delivery system by ensuring a steady therapeutic impact and minimizing the risk of dose dumping (Figure 2).

Ex-vivo mucoadhesion test

The results revealed that the mucoadhesive microspheres formulated with 220.711 mg of sodium carboxymethyl cellulose (SCMC) and 150 mg of hydroxypropyl methylcellulose (HPMC) K15M exhibited superior mucoadhesive properties compared to other formulations. This formulation demonstrated significantly improved adhesion to mucosal surfaces, highlighting the effectiveness of the polymer combination used. The enhanced mucoadhesion can be attributed to the synergistic effects of SCMC and HPMC K15M. SCMC, known for its high water absorption capacity and gel-forming abilities, contributes to the formation of a viscous layer that enhances adherence to mucosal surfaces. HPMC K15M, with its excellent film-forming properties, further supports this adhesion by creating a cohesive and stable gel matrix. The combination of these polymers likely results in a more robust mucoadhesive interface, facilitating prolonged contact with the mucosal surface. The superior mucoadhesive characteristics of this formulation are crucial for applications requiring extended interaction with the mucosa. Enhanced adhesion ensures that the microspheres remain in place longer, thereby improving the retention of the drug and enabling more effective localized drug delivery. This can lead to a more sustained therapeutic effect and potentially reduce the frequency of administration needed. Overall, the results suggest that the specific polymer combination of SCMC and HPMC K15M in this formulation significantly improves mucoadhesive properties, making it a promising candidate for applications where prolonged mucosal contact is essential for achieving optimal therapeutic outcomes (Figure 3).

Swelling assets

The study assessed the swelling characteristics of nine batches of STS mucoadhesive microspheres, designed using a central composite design. Among these formulations, F4 demonstrated the most optimal swelling behavior, with a swelling percentage of 73.07 ± 2.58% over 8 hours. All formulations exhibited swelling rates greater than 60% within the 8 hours, indicating effective water absorption and gel formation. Particularly notable was Formulation F6, which displayed higher and more consistent swelling compared to the other batches, as detailed in Table 2. The swelling percentage of the microspheres is a crucial factor influencing both the drug release rate and mucoadhesive properties. Increased swelling typically enhances the microspheres' ability to adhere to mucosal surfaces and can lead to a more controlled and sustained drug release. Therefore, formulations with higher swelling rates, such as F4 and F6, are likely to provide improved therapeutic outcomes by facilitating prolonged drug contact with the mucosa and optimizing drug delivery.

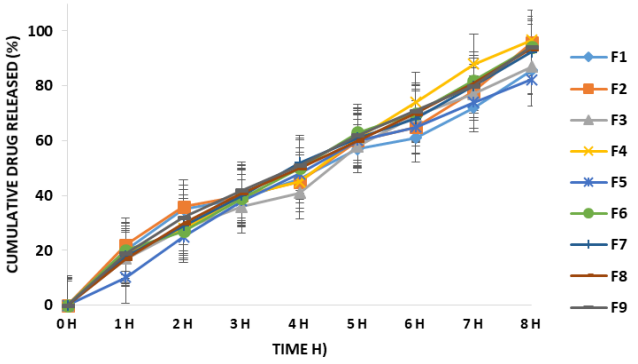

Figure 3: *In-vitro* STS discharge from the formulations

***In-vitro* Dissolution Studies**

In-vitro dissolution studies of microspheres from trials F1 to F9 provide comprehensive insights into the drug release behavior of the formulations, as illustrated in Figure 4. The studies reveal that microspheres formulated with SCMC exhibit a well-controlled drug release profile, effectively avoiding dose-dumping effects. Dose-dumping, where a large amount of drug is released in a short period, can lead to adverse effects and reduced therapeutic efficacy, making its prevention a crucial aspect of formulation development. Among the nine batches of STS mucoadhesive microspheres produced using SCMC and HPMC K15M, Formulation F6 stood out for its superior discharge characteristics. This formulation achieved a remarkable drug discharge rate of 94.07 ± 1.85 % over 8 hours. This high level of drug discharge indicates that Formulation F6 is highly effective in releasing the drug gradually and consistently, which is essential for maintaining therapeutic drug levels over extended periods. All formulations, including those other than F6, showed cumulative drug discharge rates exceeding 70% within 8 hours. However, Formulation F6 demonstrated particularly uniform and consistent drug discharge throughout the study. This uniformity is crucial as it ensures that the drug is released at a steady rate, minimizing fluctuations in drug concentration and improving therapeutic outcomes. Overall, the in vitro dissolution studies underscore the effectiveness of SCMC in achieving controlled and consistent drug release. The findings highlight Formulation F6 as the most promising candidate for applications requiring reliable and sustained drug delivery, thereby enhancing the efficacy and safety of the therapeutic regimen (Figure 3).

Analysis of %mucoadhesion

The analysis focuses on how different factors affect the % mucoadhesion of the microspheres. The final equations, which use coded factors to describe these relationships, detail how each factor influences mucoadhesive properties. The equations consider the impact of linear terms, interaction terms between factors, and quadratic terms. By evaluating these equations, one can understand how changes in the factors affect mucoadhesion and optimize the microsphere formulation to achieve the desired mucoadhesive performance.

$$\%\text{Mcoadhesive strength} = +88.00 + 0.9121A - 0.9154B + 0.2500AB + 1.69A^2 + 0.5463B^2$$

88.00 represents the intercept term of the model, representing the baseline mucoadhesive strength when all factors (X_1 and X_2) are set to zero. 0.9121A, this term shows the linear effect of factor(X_1 on mucoadhesive strength. A positive coefficient indicates that an increase in X_1 will result in an increase in mucoadhesive strength. -0.9154B, term shows the linear effect of factor X_2 on mucoadhesive strength. A negative coefficient suggests that an increase in X_2 will decrease the mucoadhesive strength. 0.2500AB: This interaction term represents the combined effect of factors X_1 and X_2 on mucoadhesive strength. The positive coefficient indicates that the interaction between X_1 and X_2 has a synergistic effect on mucoadhesive strength.1.69$A^2$is the quadratic term reflects the squared effect of factor X_1. The positive coefficient suggests that the mucoadhesive strength increases at an increasing rate as X_1 increases.0.5463B^2 is the quadratic term that reflects the squared effect of factor X_2. The positive coefficient indicates that the mucoadhesive strength increases at an increasing rate as X_2 increases. Overall, this equation allows for the prediction and optimization of mucoadhesive strength based on the levels of factors X_1 and X_2 and their interactions. It helps in understanding how these variables individually and interactively influence the outcome and guide the optimization of formulation parameters for desired mucoadhesive properties.

The ANOVA results for response Y_1, which measures mucoadhesion, indicated that several factors significantly influence the outcome. Specifically, factor A (SCMC concentration), factor B (HPMC K15M concentration), and the squared term of B (B^2) were identified as significant contributors to the response. The statistical analysis showed that these factors have a considerable impact on the mucoadhesive properties of the microspheres.

Despite the significance of these factors, the ANOVA results also revealed that the Lack of Fit for Y_1 was significant. This suggests that the current model may not perfectly fit the data, indicating that there might be other factors or interactions not accounted for in the model that influence the mucoadhesion. However, the model still demonstrated strong predictive capabilities. The Predicted R-squared value and Adequate Precision value were both 20.81, indicating that the model has a high level of predictive accuracy and a signal-to-noise ratio that is adequate for navigating the design space. Additionally, the regression coefficient (R-squared) of 0.9895 and the adjusted R-squared of 0.9721 highlight the model's robustness and reliability. These values indicate that the model explains a large portion of the variance in the response, with minimal loss of predictive power when adjusting for the number of predictors in the model. Overall, while the significant lack of fit suggests room for improvement, the high predicted R-squared and Adequate Precision values, along with the strong regression and adjusted regression coefficients, confirm that the model is effective in predicting the mucoadhesive strength of the microspheres based on the concentrations of SCMC and HPMC K15M. Further refinement of the model could involve exploring additional factors or interaction terms to improve its fit and predictive accuracy.

Optimization results

Optimization of the responses was achieved using desirability functions, a method that combines multiple responses into a single composite desirability score. This approach identified the optimal formulation parameters for achieving maximum mucoadhesion (Y_1). The optimal formulation was found to involve 146.712 mg of SCMC and 183.472 mg of HPMC K15M. This combination of ingredients resulted in the maximum mucoadhesive strength, with a desirability score of 1.0, indicating a perfect match between the predicted and desired outcomes.

The optimization process is visually represented in Figure 4, which includes contour and 3D surface plots of the overall desirability functions. These plots illustrate how varying the concentrations of SCMC and HPMC K15M within the design space affects the desirability score. The contour plots provide a two-dimensional view, showing lines of constant desirability and highlighting regions where the optimal response is achieved. The 3D surface plots offer a more comprehensive, three-dimensional view of the desirability landscape, demonstrating the interplay between the two factors and their combined effect on the overall desirability. The successful optimization underscores the critical role of SCMC and HPMC K15M concentrations in enhancing the mucoadhesive properties of the microspheres. By fine-tuning these concentrations, it is possible to achieve a formulation that maximizes mucoadhesive strength, ensuring better retention

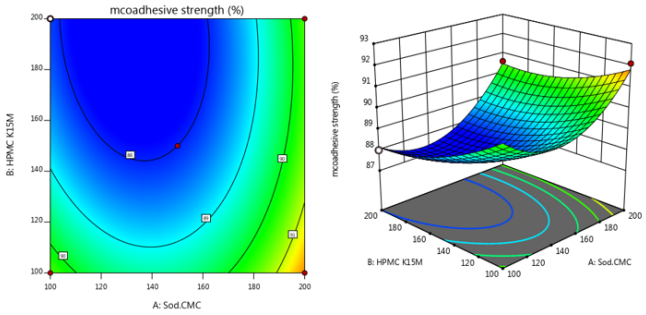

Figure 4: Contour and 3D plots for the %mucoadhesion from the polymers

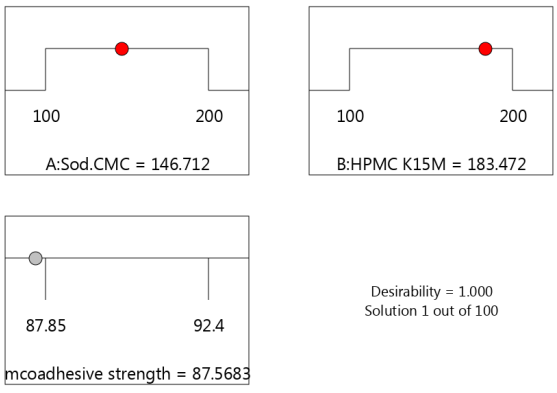

Figure 5: Optimized desirability chart

and localized drug delivery. The desirability score of 1.0 reflects the high precision and accuracy of the optimization process (Figure 5), confirming that the identified formulation parameters are indeed optimal within the experimental design space. Overall, the use of desirability functions proved to be an effective method for optimizing the formulation, ensuring that the final product meets the desired specifications for mucoadhesive strength. This approach not only identifies the best combination of ingredients but also provides a clear visual representation of how these factors interact, facilitating a deeper understanding of the formulation process and its impact on the final product's performance.

CONCLUSION

In conclusion, this study successfully developed nasal mucoadhesive microspheres of sumatriptan succinate (STS) using sodium carboxymethyl cellulose (SCMC) and hydroxyl propyl methyl cellulose (HPMC K15M) to enhance mucoadhesion. Employing a central composite design facilitated by Design Expert software, the optimal formulation was identified, containing 220.711 mg of SCMC and 150 mg of HPMC K15M. This combination demonstrated superior mucoadhesive properties and effective control over STS release. The uniform size and spherical shape of the microspheres, along with the compatibility of the polymers with STS, underscore the potential of this formulation to improve therapeutic efficacy in treating migraines and cluster headaches. These findings suggest that SCMC and HPMC K15M are promising excipients for developing effective nasal drug delivery systems for STS.

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