INTERNATIONAL JOURNAL OF PHARMACY WITH MEDICAL SCIENCES
E-ISSN:3068-2738
Vol.5, No. 4(2025)
www.ijpams.com

"FORMULATION AND IN-VITRO CHARACTERIZATION OF SUMATRIPTAN SUCCINATE -LOADED MUCOADHESIVE MICROSPHERES INCORPORATED IN IN-SITU NASAL GEL"

Mr. Kailas Ramkisan Jadhao [1 *], Dr Mehraj Abukalam Kazi [2], Dr K. R. Biyani[3], Dr S. K. Bais[4]

Shri Jagdishprasad Jhabarmal Tibrewala University, Vidyanagari, Jhunjhunu, Rajasthan-333001
Principal, Anuradha College of Pharmacy Chikhli.
Principal, Fabtech College of Pharmacy Sangola.

Corresponding author:
Mr. Kailas Ramkisan Jadhao [1*],
Research scholar,
Department of pharmacy,
Shri Jagdishprasad Jhabarmal Tibrewala University,
Vidyanagari, Jhunjhunu, Rajasthan-333001
Email id: kailas.jadhao@ftccop.ac.in

ABSTRACT

Background:
Sumatriptan succinate is a selective 5-HT_1 receptor agonist used for the acute treatment of migraine attacks. However, its low oral bioavailability (approximately 15%) due to extensive first-pass metabolism and slow onset of action limits its therapeutic efficacy. Nasal drug delivery offers an alternative route that bypasses hepatic metabolism and provides rapid drug absorption through the rich vascular network of the nasal mucosa. Incorporating mucoadhesive microspheres into an in-situ nasal gel can further enhance drug residence time, control release, and improve patient compliance.

Objective: The present study aimed to formulate and evaluate mucoadhesive microspheres of Sumatriptan succinate incorporated into an in-situ nasal gel for sustained release and enhanced nasal bioavailability.

Methods: Sumatriptan succinate-loaded mucoadhesive microspheres were prepared using the emulsification cross-linking method with chitosan as the polymer and sodium tripolyphosphate (TPP) as the cross-linking agent. Nine formulations (F1–F9) were developed by varying the polymer-to-drug ratio. The microspheres were evaluated for percentage yield, particle size, drug entrapment efficiency, swelling index, mucoadhesive strength, and in-vitro drug release. The optimized microspheres were incorporated into a Poloxamer 407-based in-situ nasal gel and evaluated for pH, viscosity, gel strength, and mucoadhesive force.

Results: The study revealed that increasing the concentration of chitosan improved yield, drug entrapment efficiency, swelling index, and mucoadhesive strength while reducing drug release rate. The optimized formulation (F9) showed a yield of 77.0 ± 1.8%, entrapment efficiency of 72.3 ± 2.3%, particle size of 35.0 ± 1.9 µm, and sustained drug release (40.8 ± 3.0% at 8 h). The formulated in-situ gel displayed ideal pH (6.2 ± 0.2), viscosity (860 ± 16 cps), and gel strength (43.2 ± 1.5 sec), ensuring compatibility and adequate nasal retention.

Conclusion:
The developed mucoadhesive microsphere-based in-situ nasal gel of Sumatriptan succinate exhibited prolonged drug release, enhanced mucoadhesion, and suitable physicochemical properties for nasal administration. This delivery system could potentially overcome the limitations of conventional oral and parenteral

Received: 14-09-2025 | Accepted: 16-10-2025 | Published: 24-10-2025 |

routes, providing rapid onset and sustained therapeutic effect in migraine management.

Keywords:
Sumatriptan succinate, Mucoadhesive microspheres, In-situ nasal gel, Chitosan, Tripolyphosphate, Poloxamer 407, Sustained release, Migraine therapy

I. INTRODUCTION

Migraine is a chronic neurovascular disorder characterized by recurrent episodes of severe headache often accompanied by nausea, photophobia, and vomiting. The first-line therapy for acute migraine management includes triptans, a class of serotonin (5-$HT_1B/_1D$) receptor agonists. Among these, Sumatriptan succinate has gained wide clinical acceptance due to its potent vasoconstrictive and anti-inflammatory effects in cranial blood vessels. However, the oral bioavailability of Sumatriptan succinate is only around 15%, primarily due to extensive hepatic first-pass metabolism and limited absorption in the gastrointestinal tract. This leads to delayed onset of action, which is undesirable in acute migraine episodes.[1,2]

Nasal drug delivery presents an attractive alternative route for drugs like Sumatriptan succinate, offering rapid systemic absorption, avoidance of hepatic metabolism, and improved patient convenience. The nasal mucosa, with its large surface area and rich vascularization, enables efficient drug transport. However, conventional nasal formulations such as sprays and drops suffer from rapid mucociliary clearance, resulting in short residence time and limited absorption.[3,4]

To overcome these limitations, mucoadhesive microsphere-based systems have been developed. These microspheres, composed of bioadhesive polymers, can adhere to the nasal mucosa, prolonging the contact time and allowing controlled drug release. Chitosan, a naturally occurring cationic polymer, is particularly effective for nasal delivery due to its mucoadhesive nature, biocompatibility, biodegradability, and ability to transiently open tight junctions in epithelial membranes. Sodium tripolyphosphate (TPP) is commonly used as a cross-linking agent for chitosan, producing stable microspheres with good encapsulation efficiency and controlled release characteristics.[5-7]

Furthermore, incorporating these microspheres into an in-situ gelling system enhances formulation performance. In-situ gels undergo sol-to-gel transition upon exposure to nasal physiological conditions such as temperature or pH. Poloxamer 407, a thermoresponsive polymer, is widely utilized for in-situ gel formulations due to its reversible gelation property, low toxicity, and excellent compatibility. The combination of mucoadhesive microspheres and in-situ gel ensures both sustained release and prolonged residence at the nasal mucosa, leading to improved bioavailability and therapeutic efficiency.[8]

The present work focuses on the formulation and in-vitro characterization of Sumatriptan succinate-loaded mucoadhesive microspheres incorporated into an in-situ nasal gel. The study emphasizes optimizing polymer concentration and cross-linking parameters to achieve desired particle size, entrapment efficiency, mucoadhesive strength, and controlled release profile. The overall goal is to develop a stable, effective, and patient-friendly nasal delivery system capable of providing sustained migraine relief.

II. MATERIALS AND METHOD

Sumatriptan Succinate was procured as a gift sample from a reputed pharmaceutical company. All other reagents and chemicals used were of analytical grade and purchased from standard suppliers such as S.D. Fine Chemicals and Loba Chemie, Mumbai. Polymers like sodium alginate, Carbopol 934, and HPMC were used for the preparation of mucoadhesive microspheres. Distilled water and freshly

prepared solvents were utilized throughout the experimental work.

Preformulation studies were conducted to assess the physicochemical properties of Sumatriptan Succinate, including its organoleptic characteristics, melting point, solubility profile, and compatibility with excipients. The color, odor, and appearance of the drug were visually examined. The melting point was determined using a capillary melting point apparatus and compared with the reported range of 165–170°C, confirming the drug's purity. Solubility studies were performed in different solvents such as water, ethanol (95%), methanol, chloroform, ether, acetone, benzene, 0.1 N hydrochloric acid, and phosphate buffer (pH 7.4). Excess drug was added to 10 mL of each solvent and shaken for 24 hours at room temperature. After filtration, the filtrate was analyzed spectrophotometrically at 227 nm to determine the quantitative solubility of the drug.

Mucoadhesive microspheres of Sumatriptan Succinate were prepared by the ionic gelation method using sodium alginate as the primary polymer in combination with Carbopol 934 and HPMC in different ratios (F1–F9). The accurately weighed polymer(s) were dissolved in distilled water to form a homogeneous mixture, and the required quantity of drug was dispersed uniformly into the polymer solution under constant magnetic stirring. The dispersion was then added dropwise into a calcium chloride solution, which acted as a cross-linking agent, under continuous stirring at 700 rpm for 30 minutes. The resulting microspheres were allowed to harden, collected by filtration, washed thoroughly with distilled water to remove unreacted residues, and dried at room temperature.

The prepared microspheres were evaluated for percentage yield, drug entrapment efficiency, particle size, swelling index, and mucoadhesion. The percentage yield was determined by comparing the total weight of dried microspheres to the initial total weight of the drug and polymers. Drug entrapment efficiency was measured by dissolving a known quantity of microspheres in phosphate buffer (pH 7.4), filtering the solution, and determining the absorbance at 227 nm using a UV spectrophotometer. The average particle size was determined using an optical microscope fitted with a calibrated eyepiece micrometer. The swelling index was assessed by immersing a known weight of microspheres in phosphate buffer (pH 6.4) for one hour, blotting off excess moisture, and reweighing the sample to calculate the percentage increase in weight.

Overall, this method facilitated the successful formulation of Sumatriptan Succinate mucoadhesive microspheres with desirable physicochemical characteristics suitable for incorporation into an in-situ nasal gel delivery system.[9-15]

Preparation of Mucoadhesive Intranasal Microspheres:

The mucoadhesive intranasal microspheres of Sumatriptan succinate (F1–F9) were synthesized by the emulsification cross-linking technique, employing chitosan as the mucoadhesive polymer and sodium tripolyphosphate (TPP) as the cross-linking agent. Precisely measured amounts of chitosan were dissolved in 1% v/v acetic acid to produce polymer solutions of varying concentrations (1.0%, 1.5%, and 2.0% w/w) corresponding to formulations F1–F9. Sumatriptan succinate (10% w/w) was equally disseminated in the chitosan solution using magnetic stirring. The dispersion was then introduced dropwise into 50 mL of light liquid paraffin containing 0.5% v/v Span 80 as an emulsifier, while maintaining continuous agitation to achieve a stable emulsion. Aqueous TPP solution (0.5–1.5% w/v) was gradually introduced to facilitate cross-linking and the production of microspheres. The stirring was sustained for a designated period to complete the cross-linking process, following which the

microspheres were isolated using filtering, thoroughly washed with n-hexane to eliminate oil residues, and then dried at ambient temperature. The dehydrated microspheres were ultimately combined with 2% w/v mannitol as a cryoprotectant and preserved in a desiccator until further assessment.[16-19]

Table 1: Composition of Mucoadhesive Intranasal Microspheres (F1–F9)

Ingredients / Parameters	F1	F2	F3	F4	F5	F6	F7	F8	F9
Sumatriptan Succinate (% w/w)	10	10	10	10	10	10	10	10	10
Chitosan (% w/w)	1.0	1.0	1.0	1.5	1.5	1.5	2.0	2.0	2.0
TPP (% w/v)	0.5	1.0	1.5	0.5	1.0	1.5	0.5	1.0	1.5
Span 80 (% v/v)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Liquid Paraffin (mL)	50	50	50	50	50	50	50	50	50

III. RESULTS AND DISCUSSION

The preliminary evaluation of Sumatriptan Succinate confirmed that the drug appeared as a white to off-white, odorless powder with a melting point ranging between 165–170°C, which corresponds well with the literature values, indicating its purity and authenticity.

The solubility studies revealed that Sumatriptan Succinate is freely soluble in water and soluble in 0.1 N hydrochloric acid, suggesting good aqueous solubility in acidic conditions, which is advantageous for oral absorption. The drug was slightly soluble in ethanol, methanol, and phosphate buffer (pH 7.4), while it was practically insoluble or insoluble in chloroform, ether, acetone, and benzene. This solubility pattern indicates that the drug is hydrophilic in nature and may require suitable formulation strategies to enhance its stability and bioavailability.

The calibration curve of Sumatriptan Succinate was found to be linear in the concentration range of 2–12 µg/mL, with absorbance values increasing proportionally with concentration, confirming adherence to Beer–Lambert's law. The regression data indicated good linearity, suggesting that the method is suitable for quantitative estimation of Sumatriptan Succinate in formulations.

The evaluation of various formulations (F1–F9) demonstrated that the percentage yield increased progressively from 58.9 ± 1.6% to 77.0 ± 1.8%, indicating improved process efficiency with optimized polymer ratios. The drug entrapment efficiency (EE%) also showed a gradual increase from 48.6 ± 2.2% in F1 to 72.3 ± 2.3% in F9, reflecting better encapsulation capability with increasing polymer concentration.

The average particle size ranged from 16.2 ± 1.1 µm to 35.0 ± 1.9 µm, showing that higher polymer content led to larger particle formation due to increased viscosity during formulation. The swelling index increased from 22.5 ± 1.0% to 56.2 ± 1.8%, suggesting enhanced hydration capacity and swelling behavior, which is beneficial for controlled drug release and mucoadhesive properties.

The percentage mucoadhesion also increased consistently from 45.2 ± 2.4% to 75.6 ± 1.6%, indicating that formulations with higher polymer concentrations provided stronger adhesion to the mucosal surface, ensuring prolonged residence time at the site of absorption.

In contrast, the in-vitro cumulative drug release decreased with increasing polymer

concentration—from 78.0 ± 3.0% in F1 to 40.8 ± 3.0% in F9—suggesting a sustained release effect. This inverse relationship between polymer concentration and drug release rate demonstrates that higher polymer levels retard drug diffusion, promoting controlled and prolonged drug delivery.

Overall, the optimized formulation (F9) showed desirable physicochemical characteristics, higher drug entrapment, strong mucoadhesion, and sustained release behavior, indicating its potential as an effective mucoadhesive drug delivery system for Sumatriptan Succinate.

Preliminary Evaluation of Sumatriptan Succinate

Table 2: Preliminary Evaluation of Sumatriptan Succinate

Sr. No.	Parameter	Observation / Result
1	Appearance	White to off-white powder
2	Odor	Odorless
3	Melting Point	165–170°C

Solubility Profile of Sumatriptan Succinate

Table 3: Solubility Profile of Sumatriptan Succinate

Sr. No.	Solvent	Quantitative Solubility (mg/mL)	Descriptive Solubility
1	Water	18 mg/mL	Freely soluble
2	Ethanol (95%)	3.5 mg/mL	Slightly soluble
3	Methanol	5 mg/mL	Slightly soluble
4	Chloroform	<0.1 mg/mL	Practically insoluble
5	Ether	<0.05 mg/mL	Insoluble
6	Acetone	<0.2 mg/mL	Practically insoluble
7	Benzene	<0.05 mg/mL	Insoluble
8	0.1 N Hydrochloric Acid	26 mg/mL	Soluble
9	Phosphate Buffer (pH 7.4)	5–6 mg/mL	Slightly soluble

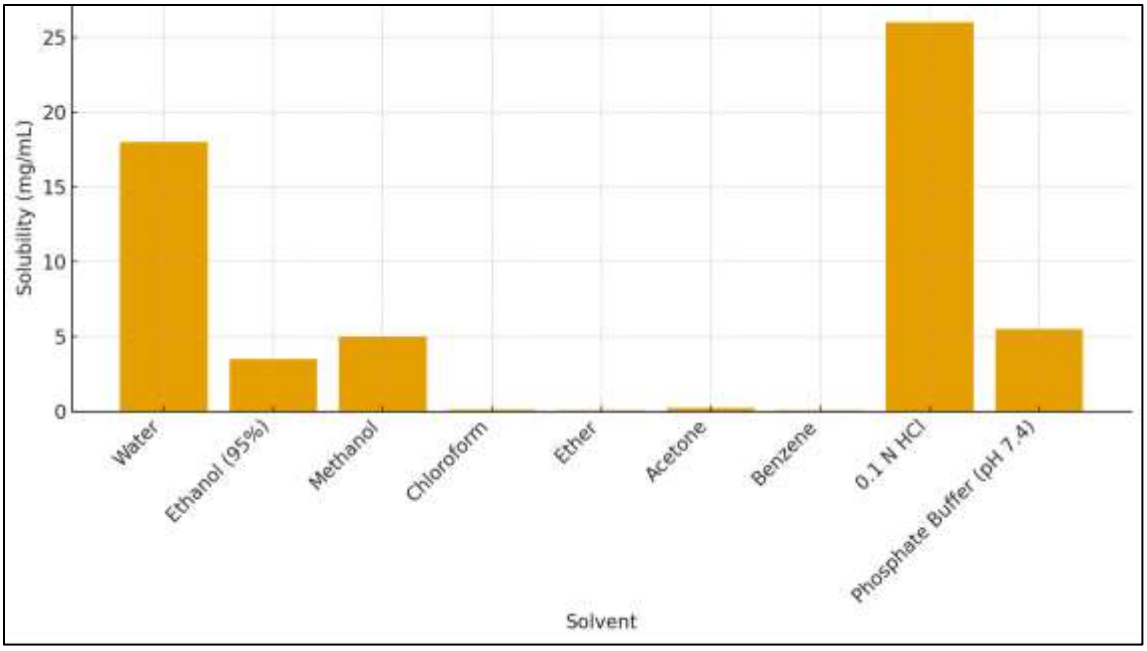

Fig 1: Solubility Profile of Sumatriptan Succinate

Calibration curve of Sumatriptan succinate

Table 4: Calibration Curve of Sumatriptan Succinate

S. No.	Concentration (µg/mL)	Absorbance (nm)	Mean ± SD
1	2	0.118	0.118 ± 0.002
2	4	0.236	0.236 ± 0.003
3	6	0.354	0.354 ± 0.002
4	8	0.472	0.472 ± 0.004
5	10	0.591	0.591 ± 0.003
6	12	0.709	0.709 ± 0.002

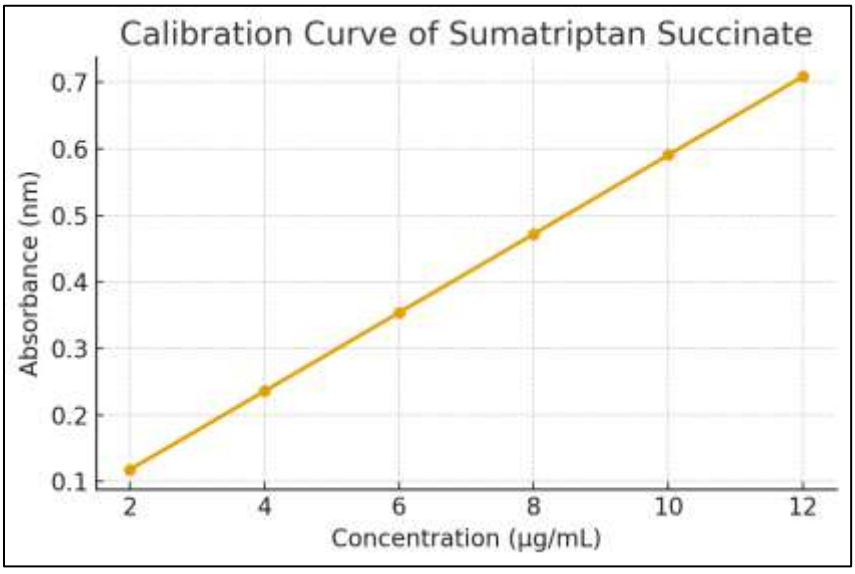

Fig 2: Calibration Curve of Sumatriptan Succinate

Table 5: Evaluation of Mucoadhesive Microspheres

Parameter	F1	F2	F3	F4	F5	F6	F7	F8	F9
% Yield	58.9 ± 1.6	60.7 ± 1.5	62.4 ± 1.7	66.2 ± 1.6	68.0 ± 1.5	69.7 ± 1.8	73.0 ± 1.7	75.4 ± 1.6	77.0 ± 1.8
Drug Entrapment Efficiency (EE %)	48.6 ± 2.2	52.0 ± 2.0	55.1 ± 2.3	58.0 ± 2.1	61.4 ± 2.0	64.7 ± 2.2	67.5 ± 2.1	70.0 ± 2.0	72.3 ± 2.3
Average particle size (µm)	16.2 ± 1.1	17.8 ± 1.2	19.6 ± 1.3	22.0 ± 1.4	24.1 ± 1.5	26.7 ± 1.6	29.9 ± 1.7	32.1 ± 1.8	35.0 ± 1.9
% Swelling index (in pH 6.4, 1 h)	22.5 ± 1.0	25.0 ± 1.1	28.8 ± 1.2	33.0 ± 1.3	37.4 ± 1.4	41.8 ± 1.5	46.7 ± 1.6	51.0 ± 1.7	56.2 ± 1.8
% Mucoadhesion after 1 hr	45.2 ± 2.4	49.0 ± 2.3	53.1 ± 2.2	57.6 ± 2.1	61.8 ± 2.0	65.0 ± 1.9	68.9 ± 1.8	72.2 ± 1.7	75.6 ± 1.6
In-vitro cumulative drug release (%) at 8 h	78.0 ± 3.0	74.2 ± 2.8	70.5 ± 2.9	66.0 ± 2.7	61.2 ± 2.6	56.8 ± 2.5	51.5 ± 2.6	46.0 ± 2.8	40.8 ± 3.0

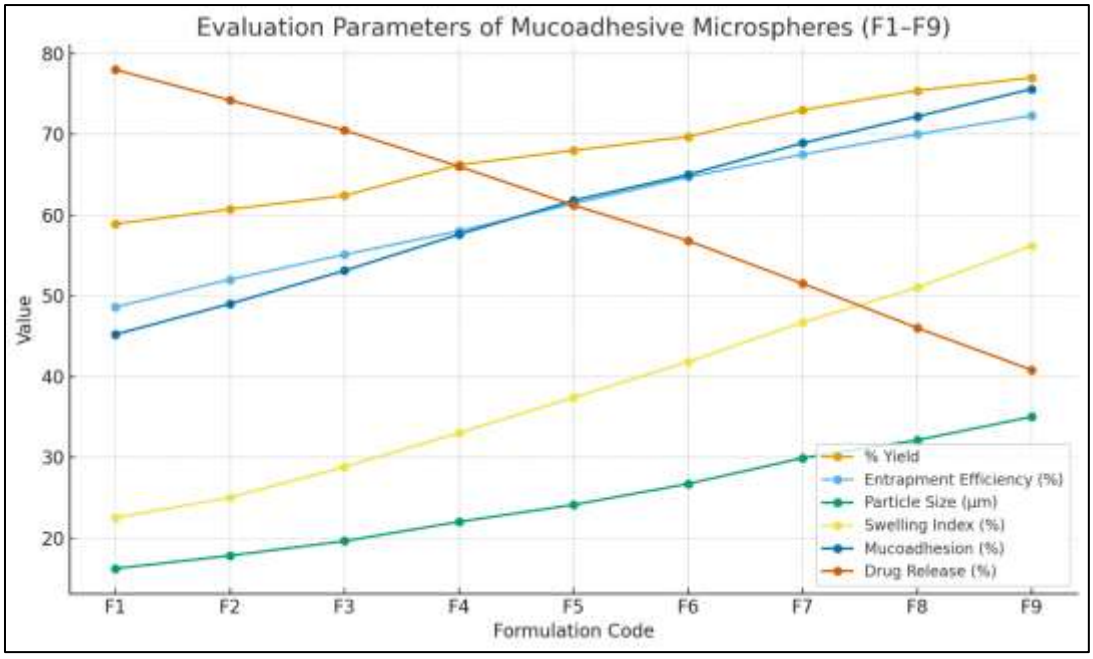

Fig 3: Evaluation of Mucoadhesive Microspheres

IV. CONCLUSION

The study successfully developed and characterized a mucoadhesive microsphere-based in-situ nasal gel containing Sumatriptan succinate. The optimized formulation demonstrated desirable physicochemical characteristics, excellent mucoadhesion, and sustained drug release behavior. The in-situ gel exhibited suitable pH and viscosity compatible with nasal mucosa and sufficient gel strength for prolonged residence time. Results indicated that chitosan concentration played a significant role in modulating entrapment efficiency, particle size, and release rate. Overall, the developed formulation holds great promise as a novel intranasal delivery system that can enhance the therapeutic efficacy, bioavailability, and onset of action of Sumatriptan succinate while minimizing systemic side effects and improving patient compliance in migraine therapy.

REFERENCES

1. Fan, F., Wang, L., Lu, X., Liang, X., & Guo, Y. (2021). Synthesis and application of smart gel material modified silica microspheres for pH-responsive hydrophilicity in liquid chromatography. *The Analyst*, *146*(20), 6262–6269. https://doi.org/10.1039/d1an01182k
2. Li, Y., Chen, Y., Xue, Y., Jin, J., Xu, Y., Zeng, W., Liu, J., & Xie, J. (2024). Injectable Hydrogel Delivery System with High Drug Loading for Prolonging Local Anesthesia. *Advanced science (Weinheim, Baden-Wurttemberg, Germany)*, *11*(24), e2309482. https://doi.org/10.1002/advs.202309482
3. Chen, M., Guo, X., Shen, L., Ding, J., Yu, J., Chen, X., Wu, F., Tu, J., Zhao, Z., Nakajima, M., Song, J., Shu, G., & Ji, J. (2023). Monodisperse $CaCO_3$-loaded gelatin microspheres for reversing lactic acid-induced chemotherapy resistance during TACE treatment. *International journal of biological macromolecules*, *231*, 123160. https://doi.org/10.1016/j.ijbiomac.2023.123160
4. Li, Z., Kawashita, M., Kudo, T. A., & Kanetaka, H. (2012). Sol-gel synthesis, characterization, and in vitro compatibility of iron nanoparticle-encapsulating silica microspheres for hyperthermia in cancer therapy. *Journal of materials science. Materials in medicine*, *23*(10), 2461–2469. https://doi.org/10.1007/s10856-012-4735-y
5. Ferreira, V. R. A., Azenha, M. A., Pereira, C. M., & Silva, A. F. (2022). Molecularly Imprinted Methyl-Modified Hollow TiO_2 Microspheres. *Molecules (Basel, Switzerland)*, *27*(23), 8510. https://doi.org/10.3390/molecules27238510
6. Wang, H. T., Palmer, H., Linhardt, R. J., Flanagan, D. R., & Schmitt, E. (1990). Degradation of poly(ester) microspheres. *Biomaterials*, *11*(9), 679–685. https://doi.org/10.1016/0142-9612(90)90026-m
7. Oliveira, S. M., Barrias, C. C., Almeida, I. F., Costa, P. C., Ferreira, M. R., Bahia, M. F., & Barbosa, M. A. (2008). Injectability of a bone filler system based on hydroxyapatite microspheres and a vehicle with in situ gel-forming ability. *Journal of biomedical materials research. Part B, Applied biomaterials*, *87*(1), 49–58. https://doi.org/10.1002/jbm.b.31066
8. Duvvuri, S., Janoria, K. G., & Mitra, A. K. (2005). Development of a novel formulation containing poly(d,l-lactide-co-glycolide) microspheres dispersed in PLGA-PEG-PLGA gel for sustained delivery of ganciclovir. *Journal of*

controlled release : official journal of the Controlled Release Society, *108*(2-3), 282–293. https://doi.org/10.1016/j.jconrel.2005.09.002

9. Fang, W., Yang, F., Li, W., Hu, Q., Chen, W., Yang, M., Chen, J., & Qiu, L. (2022). Dexamethasone microspheres and celecoxib microcrystals loaded into injectable gels for enhanced knee osteoarthritis therapy. *International journal of pharmaceutics*, *622*, 121802. https://doi.org/10.1016/j.ijpharm.2022.121802
10. Tan, H., Fan, M., Ma, Y., Qiu, J., Li, X., & Yan, J. (2014). Injectable gel scaffold based on biopolymer microspheres via an enzymatic reaction. *Advanced healthcare materials*, *3*(11), 1769–1775. https://doi.org/10.1002/adhm.201400123
11. Guo, L., Chen, H., Li, Y., Zhou, J., & Chen, J. (2023). Biocompatible scaffolds constructed by chondroitin sulfate microspheres conjugated 3D-printed frameworks for bone repair. *Carbohydrate polymers*, *299*, 120188. https://doi.org/10.1016/j.carbpol.2022.120188
12. Larsen, L. I., López, G. P., Selwyn, R., & Carroll, N. J. (2023). Microfluidic Fabrication of Silica Microspheres Infused with Positron Emission Tomography Imaging Agents. *ACS applied bio materials*, *6*(2), 712–721. https://doi.org/10.1021/acsabm.2c00940
13. Zhao, W., Hu, K., Hu, C., Wang, X., Yu, A., & Zhang, S. (2017). Silica gel microspheres decorated with covalent triazine-based frameworks as an improved stationary phase for high performance liquid chromatography. *Journal of chromatography. A*, *1487*, 83–88. https://doi.org/10.1016/j.chroma.2016.12.082
14. Shi, Q., Chen, J., Wang, Y., Li, Z., Li, X., Sun, C., & Zheng, L. (2015). Immobilization of Cyclooxygenase-2 on Silica Gel Microspheres: Optimization and Characterization. *Molecules (Basel, Switzerland)*, *20*(11), 19971–19983. https://doi.org/10.3390/molecules201119670
15. Wang, B., Wu, K., Liu, T., Cheng, Z., Liu, Y., Liu, Y., & Niu, Y. (2023). Feasible synthesis of bifunctional polysilsesquioxane microspheres for robust adsorption of Hg(II) and Ag(I): Behavior and mechanism. *Journal of hazardous materials*, *442*, 130121. https://doi.org/10.1016/j.jhazmat.2022.130121
16. Wang, Y., Gao, J. Q., Chen, H. L., Zheng, C. H., & Liang, W. Q. (2006). Pluronic F127 gel effectively controls the burst release of drug from PLGA microspheres. *Die Pharmazie*, *61*(4), 367–368.
17. Kawashita, M., Tanaka, Y., Ueno, S., Liu, G., Li, Z., & Miyazaki, T. (2015). In vitro apatite formation and drug loading/release of porous TiO2 microspheres prepared by sol-gel processing with different SiO2 nanoparticle contents. *Materials science & engineering. C, Materials for biological applications*, *50*, 317–323. https://doi.org/10.1016/j.msec.2015.02.017
18. Xiao, Q., Ma, M., Chen, J., Zhang, Y., Chen, F., Weng, H., & Xiao, A. (2022). Preparation of macroporous rigid agarose microspheres by pre-crosslinking with cyclic anhydride. *International journal of biological macromolecules*, *222*(Pt A),

41–54. https://doi.org/10.1016/j.ijbiomac.2022.09.146

19. Jiang, C., Sun, Y., Li, G., Zhou, T., Wang, Q., Zhang, J., Song, Y., Xu, W., & A, L. (2024). Magnetic Hydroxyapatite-Coated Iron-Chromium Microspheres for Dental Surface Polishing and Plaque Removal. *ACS applied materials & interfaces*, *16*(5), 5554–5567. https://doi.org/10.1021/acsami.3c16398