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Formulation and Evaluation of Clopidogrel Bisulphate Microspheres Using HPMC Polymer

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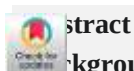
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Abstract

Background: Clopidogrel bisulphate is an antiplatelet agent used in the prevention of atherothrombotic events. Polymeric microspheres offer a potential approach for modifying drug-release behaviour and improving formulation performance. The present study aimed to formulate and evaluate clopidogrel bisulphate-loaded hydroxypropyl methylcellulose (HPMC) microspheres.

Methods: Clopidogrel bisulphate-loaded HPMC microspheres were prepared using the solvent extraction method. The prepared formulations (F1–F5) were evaluated for micromeritic properties, particle size, zeta potential, percentage yield, drug encapsulation efficiency, drug-loading capacity and in-vitro drug release. A UV spectrophotometric calibration curve was established over the concentration range of 4–40 µg/mL at 240 nm.

Results: The percentage yield ranged from 80.73% to 97.37%, while encapsulation efficiency ranged from 68.59% to 78.10%. Drug-loading capacity varied from 30.98% to 49.21%. The reported particle-size values ranged from 0.3652 to 0.7832 µm, and zeta potential values ranged from –23.22 to –29.76 mV. Among the evaluated formulations, F3 showed the highest reported cumulative drug release at 24 hours (95.56%), compared with F1 (73.21%), F2 (82.22%), F4 (89.22%) and F5 (86.90%).

Conclusion: Clopidogrel bisulphate-loaded HPMC microspheres were successfully prepared and evaluated. Based on the reported in-vitro drug-release results, F3 was identified as the best-performing formulation among those studied. Further investigation, including confirmation of formulation composition, detailed release-kinetic analysis and appropriate stability and pharmacokinetic studies, is required to establish its overall performance.

Keywords: Clopidogrel bisulphate; HPMC; microspheres; solvent extraction; encapsulation efficiency; in-vitro drug release.

1. INTRODUCTION

Clopidogrel bisulphate is an orally administered thienopyridine antiplatelet prodrug used to reduce atherothrombotic events. Its pharmacological activity depends on metabolic activation, and its formulation

performance is influenced by dissolution, gastrointestinal conditions and first-pass metabolism. Published formulation studies have explored controlled-release and gastroretentive approaches for clopidogrel bisulphate, including HPMC-containing floating tablets and multiparticulate systems; these reports establish formulation precedent but do not establish clinical superiority for the microspheres investigated here^[1–5].

Microspheres are particulate drug carriers in which an active ingredient is distributed within a polymeric matrix or contained in a polymer-rich structure. They can be designed to modify drug-release rate, protect the incorporated drug and provide a reproducible multiparticulate dosage form. Particle size, porosity, drug distribution, polymer composition and manufacturing conditions can affect encapsulation efficiency, morphology and release behaviour^[6–10]. These outcomes must be established experimentally for each formulation rather than assumed from the delivery platform alone.

Hydroxypropyl methylcellulose (HPMC; hypromellose) is a cellulose-derived pharmaceutical excipient used in modified-release formulations. On hydration, HPMC can form a viscous polymer-rich layer that influences diffusion, swelling and erosion; polymer grade, viscosity, concentration and excipient composition may change the resulting release profile^[11–15]. Although much of this mechanistic literature concerns HPMC matrix tablets, it provides relevant background for considering polymer concentration as a formulation variable. The behaviour of HPMC in the present microspheres is interpreted from the measured results only.

Emulsion-based solvent extraction or evaporation methods form dispersed droplets containing drug and polymer, followed by solvent removal or extraction to solidify the particles. Stirring rate, dispersed-phase composition, external-phase volume, surfactant concentration and solvent-removal conditions can influence particle size, surface morphology, yield and drug release^[7–10,16–20]. Because process sensitivity varies with the polymer–solvent system, the exact conditions and washing/drying steps should be reported clearly. The preparation method below follows the experimental description in the supplied dissertation; details not documented there have not been added.

The present study aimed to prepare clopidogrel bisulphate-loaded HPMC microspheres by the solvent-extraction method and evaluate their physicochemical characteristics and in-vitro drug release. The study assessed five drug–polymer compositions and compared micromeritic properties, particle size, zeta potential, morphology, production yield, encapsulation efficiency, loading capacity and in-vitro release. This is an in-vitro formulation study; no claim of improved human bioavailability or clinical benefit is made without supporting in-vivo evidence.

2. MATERIALS AND METHODS

2.1 Materials

Clopidogrel bisulphate was obtained from Microlabs Pvt. Ltd., Kolar. HPMC, ethyl acetate, polyvinyl alcohol, glacial acetic acid, light and heavy liquid paraffin, n-hexane and Tween 80 were listed in the dissertation as materials used or available for the work. The preparation procedure specifically reports HPMC, 5% acetic acid, light and heavy liquid paraffin, Tween 80, aqueous glutaraldehyde and n-hexane. Supplier names, grades and batch numbers should be completed from laboratory records where available; they are not inferred here. The choice of HPMC and emulsion-processing conditions is consistent with the general formulation literature on HPMC-based release systems and polymeric microspheres^[11–20].

2.2 Preformulation

Melting point was determined by the capillary method. Solubility was assessed in water, 0.1 N HCl and alcohol; the dissertation also describes solubility in acetone, methylene chloride and ethyl ether. FTIR compatibility assessment was performed for pure clopidogrel bisulphate, HPMC and their physical mixture using KBr pellets scanned over 450–4000 cm⁻¹. DSC samples (approximately 2–6 mg) were sealed in aluminium pans and heated at 10°C/min under nitrogen at 40 mL/min.

2.3 UV Calibration Curve

Clopidogrel bisulphate was quantified spectrophotometrically at 240 nm. A 1000 µg/mL stock solution was prepared in 0.1 N HCl and diluted to standards spanning 4–40 µg/mL. Absorbance was recorded using 0.1 N HCl as the blank. The calibration values and reported regression statistic are retained from the dissertation; the regression statistic should be confirmed as the coefficient of determination (R²) from the original instrument output before submission. Quantification of drug content and release should be validated for specificity and linearity in the relevant sample matrix^[24,25].

2.4 Preparation of Microspheres

The thesis describes dissolving HPMC and clopidogrel bisulphate in 5% acetic acid, followed by addition of the drug–polymer dispersion to liquid paraffin containing Tween 80 under mechanical stirring at 1500 rpm. Glutaraldehyde solution was added during stirring, and the dispersion was stirred for a total of approximately 2 h. The microspheres were allowed to settle, collected by filtration, washed with n-hexane to remove oil and water to remove excess glutaraldehyde, and dried at 40°C for 24 h.

Note on source consistency: the method text states 150 mg drug in the preparation paragraph, while the formulation table specifies 200 mg drug for F1–F5. This manuscript preserves the formulation table values; the discrepancy should be confirmed against laboratory records before submission.

2.5 Formulation Design

Five formulations (F1–F5) were described in the source formulation table with 200 mg clopidogrel bisulphate and increasing HPMC quantities of 100, 200, 300, 400 and 500 mg, respectively. The reported drug-to-polymer ratios in the source table are retained. A separate preparation paragraph in the dissertation states 150 mg of drug; this conflicts with the table and must be resolved against the original laboratory notebook before final publication. The present manuscript uses the table values for comparative reporting and does not silently reconcile the discrepancy.

Table 1. Composition of clopidogrel bisulphate-loaded HPMC microspheres.

Formulation n	Clopidogrel bisulphate (mg)	HPMC (mg)	Drug:polymer ratio
F1	200	100	2:1
F2	200	200	2:2
F3	200	300	2:3
F4	200	400	2:4
F5	200	500	2:5

2.6 Evaluation of Microspheres

Micromeritic properties included bulk density, Carr's compressibility index, Hausner ratio and angle of repose. Angle of repose was determined using the fixed-funnel method. Bulk and tapped densities were used to calculate Carr's index and Hausner ratio. The use of these powder-flow measures is consistent with common characterization practice for multiparticulate formulations [6,8,10].

Particle size and zeta potential were determined using a zeta/particle-size analyser after dilution of the formulation. Surface morphology was examined by scanning electron microscopy (SEM); the sample was mounted on a stub, coated with platinum and imaged under high vacuum. Particle size and surface morphology are important process-dependent attributes in emulsion-prepared microspheres [7–10,16–20].

Percentage yield was calculated as the weight of recovered microspheres divided by the total weight of drug and polymer used, multiplied by 100. For encapsulation efficiency and loading capacity, a weighed quantity of microspheres was extracted in pH 1.2 medium for 24 h, centrifuged at 6000 rpm for 30 min and filtered. The filtrate was appropriately diluted and analysed at 240 nm. The source document provides the equations and reports the resulting formulation values. Yield, encapsulation efficiency and loading capacity are standard comparative responses in microsphere formulation studies [7–10,16–20].

In-vitro drug release was studied using USP basket apparatus (Type I) with 900 mL of 0.1 N HCl at 37°C. Aliquots were withdrawn at specified intervals and replaced with equal volumes of fresh medium. Drug concentration was measured spectrophotometrically at 240 nm. Release data were assessed using zero-order, first-order, Higuchi and Peppas models. The release data were considered in relation to established diffusion and polymer-controlled release models; model fit alone should not be treated as proof of a unique mechanism [11–15,24,25].

3. RESULTS

3.1 Preformulation and UV Calibration

The dissertation reports a melting-point range of 184–194°C for clopidogrel bisulphate. The drug was described as highly soluble in 0.1 N HCl, practically insoluble in water at neutral pH, freely soluble in methanol, sparingly soluble in methylene chloride and practically insoluble in ethyl ether. The standard calibration curve covered 4–40 µg/mL at 240 nm, with a reported slope of 0.018 and regression value of 0.997 (Figure 1).

Table 2. Standard calibration data for clopidogrel bisulphate at 240 nm.

Concentration (µg/mL)	Absorbance
4	0.079
8	0.152
12	0.231
16	0.315
20	0.376
24	0.443
28	0.529
32	0.624
36	0.66
40	0.727

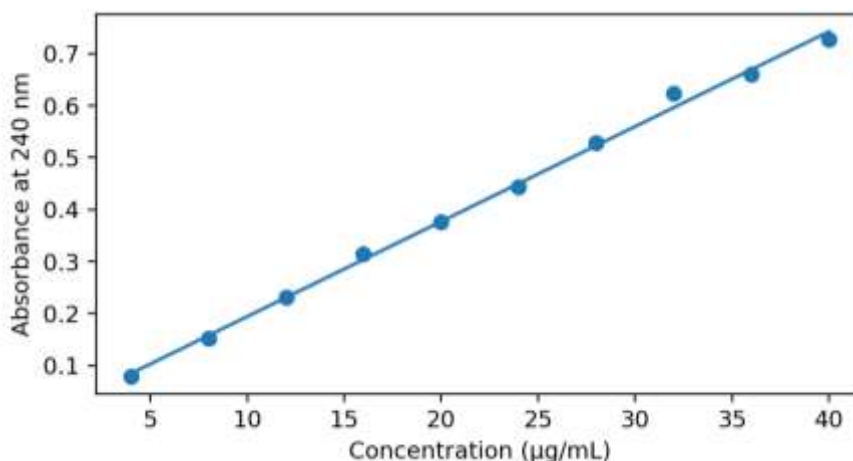


Fig 1: Standard calibration curve of clopidogrel bisulphate at 240 nm.

3.2 Drug–Polymer Compatibility

FTIR spectra of pure clopidogrel bisulphate, HPMC and their physical mixture retained the characteristic spectral features reported in the dissertation, without major appearance or disappearance of bands. This was interpreted by the source authors as indicating no major physical incompatibility between the drug and polymer (Figure 2).

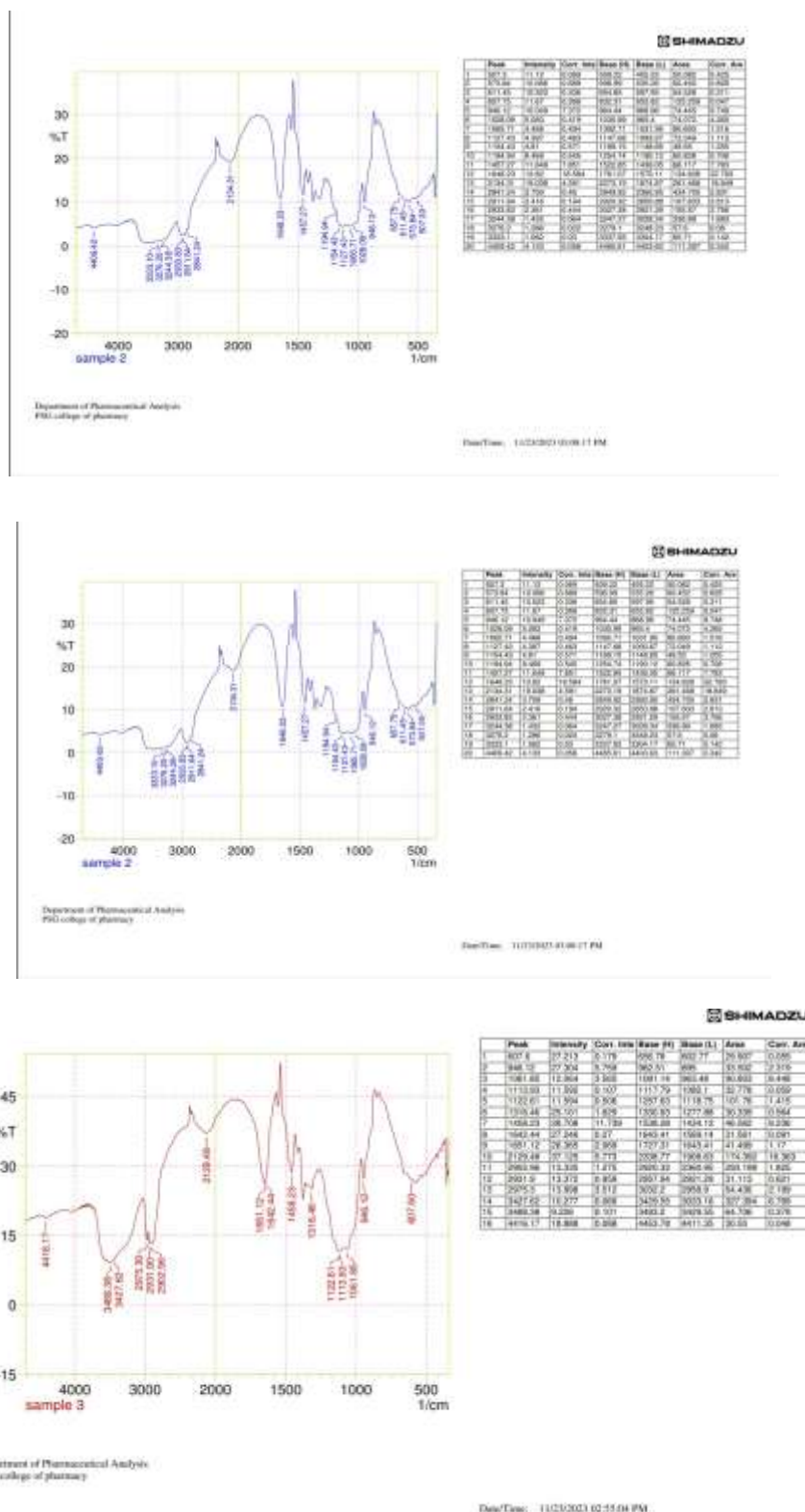
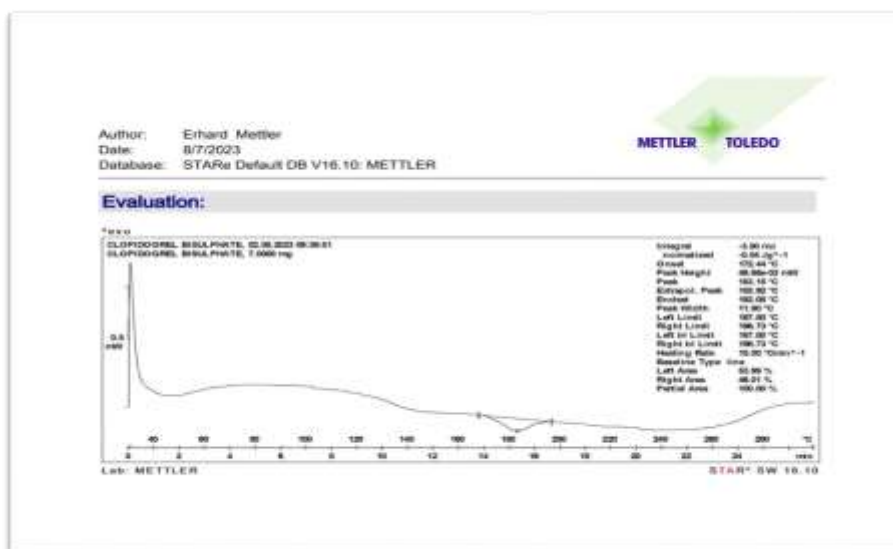


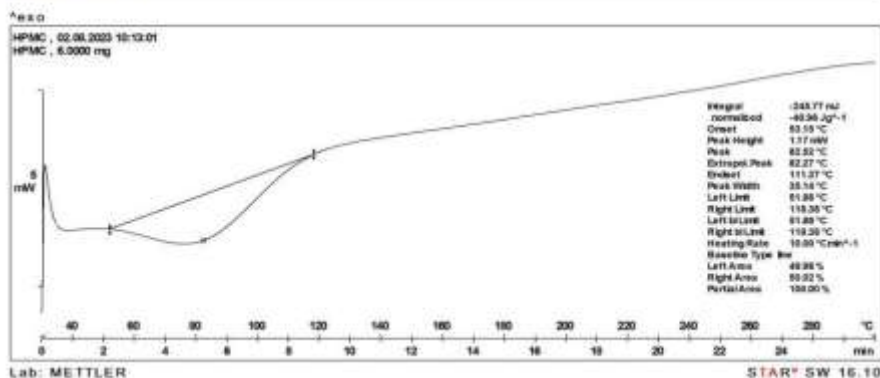
Fig 2: Composite FTIR spectra: (A) clopidogrel bisulphate, (B) HPMC and (C) physical mixture.

DSC thermograms reported characteristic peaks at 183.15°C and 192.08°C for clopidogrel bisulphate, while HPMC showed a thermal feature reported around 82.5°C. The physical mixture retained drug-associated thermal peaks, which the dissertation interpreted as indicating no major drug-polymer interaction (Figure 3). The original thesis contains typographical uncertainty in the HPMC peak temperature; the value should be checked against the instrument report.



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Evaluation:



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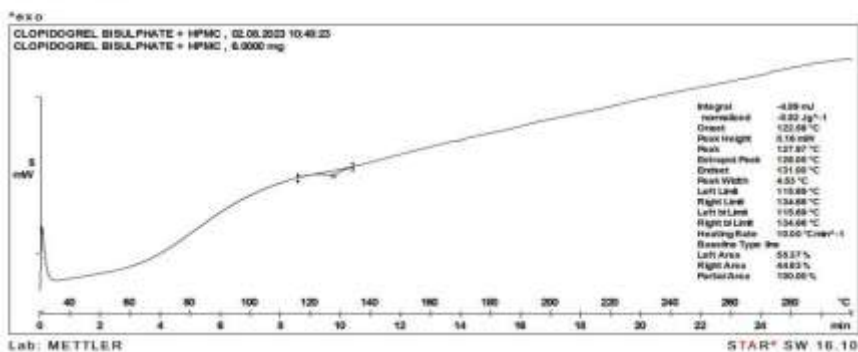


Fig 3: Composite DSC thermograms: (A) clopidogrel bisulphate, (B) HPMC and (C) physical mixture.

3.3 Micromeritic Properties

Micromeritic characteristics varied across the five batches. Bulk density ranged from 0.186 to 0.372 g/mL. Carr's index ranged from 8.16% to 15.23%, Hausner ratio from 1.09 to 1.21, and angle of repose from 22.82° to 28.69°. The values indicate that powder-flow behaviour varied with polymer content, with F1 showing the lowest Carr's index and Hausner ratio among the tested batches.

Table 3. Micromeritic properties of clopidogrel bisulphate-loaded HPMC microspheres.

Formulation	Bulk density (g/mL)	Carr's index (%)	Hausner ratio	Angle of repose (°)
F1	0.186 ± 0.01	8.16 ± 0.13	1.09 ± 0.06	22.82 ± 0.21
F2	0.307 ± 0.02	9.71 ± 0.17	1.16 ± 0.03	23.68 ± 0.63
F3	0.372 ± 0.01	10.8 ± 0.09	1.19 ± 0.07	24.64 ± 0.55
F4	0.371 ± 0.03	14.9 ± 0.21	1.21 ± 0.08	26.81 ± 0.41
F5	0.332 ± 0.02	15.23 ± 0.19	1.19 ± 0.05	28.69 ± 0.37

3.4 Particle Size and Zeta Potential

The mean particle size increased with increasing HPMC concentration, from 0.3652 µm for F1 to 0.7832 µm for F5. The zeta potential ranged from -23.22 to -29.76 mV. The source thesis reports increasingly negative zeta-potential values as polymer amount increased. These results indicate that polymer concentration was associated with changes in particle dimensions and measured surface charge.

Table 4. Particle size and zeta potential of clopidogrel bisulphate-loaded HPMC microspheres.

Formulation	Mean particle size (µm)	Zeta potential (mV)
F1	0.3652	-23.22
F2	0.4886	-24.78
F3	0.5218	-26.70
F4	0.6437	-28.01
F5	0.7832	-29.76

3.5 Surface Morphology

SEM examination of the selected F3 formulation showed microspheres with a predominantly spherical appearance and a comparatively smooth, dense surface, as described in the dissertation. The morphology was consistent with formation of a particulate polymeric matrix. The source SEM image is reproduced in Figure 4.

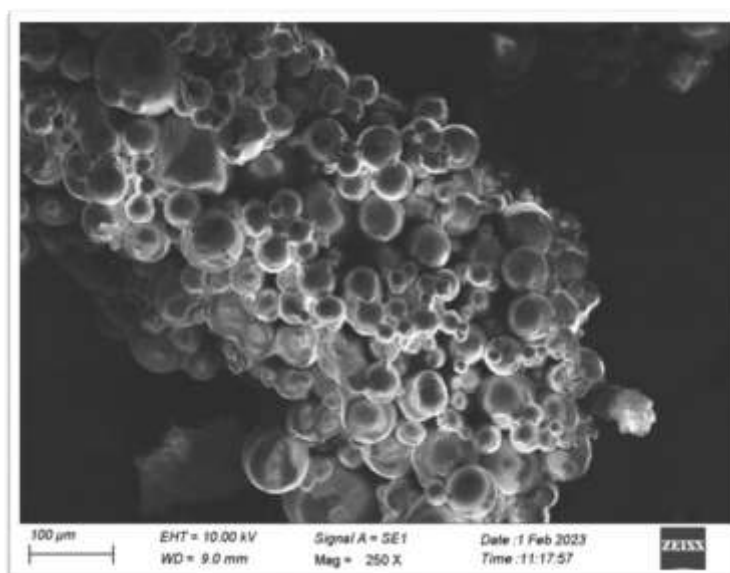


Fig 4. SEM micrograph of clopidogrel bisulphate-loaded HPMC microspheres (source thesis image).**3.6 Percentage Yield, Encapsulation Efficiency and Loading Capacity**

Percentage yield increased from 80.73% to 97.37% as the polymer amount increased from F1 to F5. Encapsulation efficiency increased from 68.59% to 78.10%, whereas loading capacity decreased from 49.21% to 30.98%. F5 showed the highest yield and encapsulation efficiency, while F1 showed the highest loading capacity.

Table 5. Yield, encapsulation efficiency and loading capacity of microspheres.

Formulation n	Yield (%)	Encapsulation efficiency (%)	Loading capacity (%)
F1	80.73	68.59	49.21
F2	86.50	71.04	43.32
F3	90.51	74.89	36.43
F4	93.63	75.69	33.25
F5	97.37	78.10	30.98

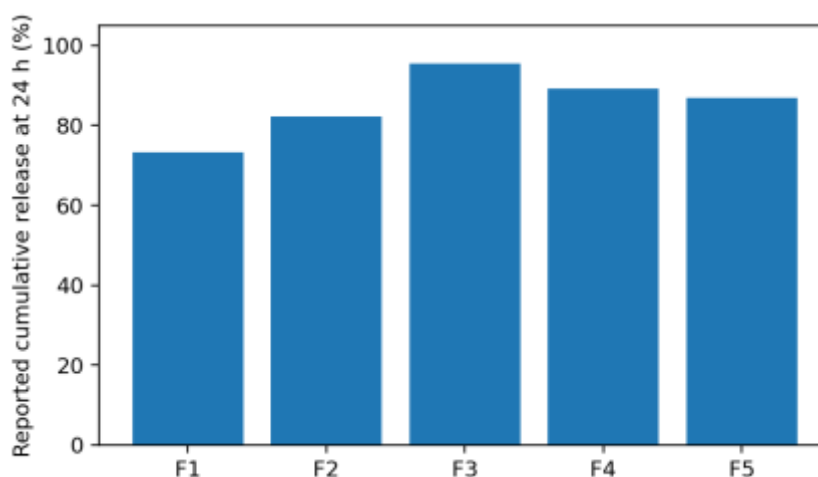
The inverse trend between polymer amount and loading capacity is consistent with increasing polymer mass contributing a larger proportion of the total microsphere mass. These data demonstrate that selecting an optimized formulation requires balancing encapsulation efficiency and yield against drug loading and release performance.

3.7 In-Vitro Drug Release

The in-vitro release study was conducted over 24 h in 900 mL of 0.1 N HCl at 37°C using USP basket apparatus. The dissertation reports first-hour release values of 24.84%, 26.01%, 27.53%, 20.07% and 17.52% for F1–F5, respectively. The reported 24-h cumulative release values were 73.21%, 82.22%, 95.56%, 89.22%, 86.90%, respectively.

Table 6. Reported cumulative drug release values at 1 h and 24 h.

Formulation n	Release at 1 h (%)	Release at 24 h (%)
F1	24.84	73.21
F2	26.01	82.22
F3	27.53	95.56
F4	20.07	89.22
F5	17.52	86.90

**Fig 5.** Comparison of reported 24-h cumulative drug release across formulations.

F3 showed the highest reported 24-h release (95.56%) and was identified as the optimized formulation in the results section of the thesis. The source document contains a conflicting value of 96.98% in its summary; the raw dissolution dataset should be checked to resolve this difference before submission.

3.8 Release Kinetics

The release data were analysed using zero-order, first-order, Higuchi and Peppas/Ritger–Peppas models. The dissertation describes the release profile as fitting the Higuchi and zero-order models and reports a non-Fickian mechanism. However, numerical regression coefficients and the release exponent for each formulation were not consistently provided in the accessible results text. Accordingly, no unsupported R^2 or exponent values are inserted here.

3.9 Summary of Principal Evaluation Results

Table 7. Summary of the principal findings for clopidogrel bisulphate-loaded HPMC microspheres.

Evaluation	Principal result from source thesis
Melting point	184–194°C
UV calibration	4–40 µg/mL at 240 nm; slope $\approx$ 0.018; regression value 0.997
Micromeritic properties	Carr's index 8.16–15.23%; Hausner ratio 1.09–1.21; angle of repose 22.82–28.69°
Particle size	0.3652–0.7832 µm
Zeta potential	–23.22 to –29.76 mV
Yield	80.73–97.37%
Encapsulation efficiency	68.59–78.10%
Loading capacity	30.98–49.21%
24-h release	73.21–95.56% reported in Results section
Formulation selected	F3, based on the reported 24-h release profile

3.10 Stability

The thesis states that F3 was selected for stability studies, but the accessible source text did not provide a complete stability dataset with storage conditions, time points and quantitative changes. A stability claim cannot therefore be quantified in this manuscript without the corresponding results table or raw records.

4. DISCUSSION

This study investigated clopidogrel bisulphate-loaded HPMC microspheres prepared by a solvent-extraction approach. The evaluation results show that HPMC concentration affected particle size, surface charge, production yield, encapsulation efficiency, loading capacity and in-vitro release. These relationships are consistent with the established role of polymer composition and processing conditions in determining microsphere formation and drug transport^[6–10,20,23–25]. Clopidogrel formulation studies have likewise shown that polymer selection and dosage-form design can influence release behaviour, although results from floating tablets or other microcarriers cannot be assumed to predict the performance of the present HPMC microspheres^[1,3–5].

FTIR and DSC results were interpreted in the dissertation as showing no major incompatibility between clopidogrel bisulphate and HPMC. The preservation of characteristic drug-associated bands and thermal features supports physical compatibility under the test conditions, although FTIR/DSC alone cannot exclude every possible chemical or physical interaction. Similar compatibility assessments have been reported for clopidogrel-containing multiparticulate systems^[3,5]. These observations should be considered alongside stability-indicating analytical data in future work.

Increasing the HPMC amount was associated with larger particles and higher production yield and encapsulation efficiency. Yield increased from 80.73% to 97.37%, while encapsulation efficiency rose from 68.59% to 78.10%. In contrast, loading capacity declined from 49.21% to 30.98%, reflecting the increasing proportion of polymer in the recovered product. This trade-off illustrates why a high yield or

entrapment value alone is not sufficient to define the optimum formulation; polymer-to-drug ratio and process conditions are known to influence microsphere characteristics and encapsulation outcomes [6–10,20,23–25].

The particle size increased from 0.3652 μm in F1 to 0.7832 μm in F5. A higher polymer fraction can increase dispersed-phase viscosity and contribute to larger particles under otherwise similar processing conditions, although this explanation remains a mechanistic interpretation and would require process-viscosity data for confirmation in this study [7–10,24,25]. Zeta potential values were negative across the batches, ranging from –23.22 to –29.76 mV. These measurements describe the tested dispersions, but zeta potential alone should not be treated as definitive proof of long-term physical stability.

The in-vitro release profile showed an initial release during the first hour followed by continued release over 24 h. F3 had the highest reported cumulative 24-h release (95.56%), and the dissertation selected F3 as the optimized batch. Clopidogrel formulation studies and polymeric controlled-release literature similarly demonstrate that polymer type, polymer concentration and carrier architecture can alter dissolution behaviour [1–4,6,11,12,15,17]. However, the reported endpoint values alone do not establish a specific release mechanism; this interpretation should be supported by complete time-point data and model-fit statistics.

HPMC can regulate release through hydration and formation of a viscous polymeric layer, which can slow mass transport and alter the balance between diffusion, swelling and polymer relaxation [11,12,14,15,17–19]. The source thesis describes the release profile as consistent with Higuchi/zero-order behaviour and non-Fickian diffusion. Because the numerical model-fit values are not fully reported in the available source text, the present manuscript retains that qualitative interpretation without assigning unsupported correlation coefficients or release exponents. Release models should be compared using the complete dissolution dataset and appropriate model assumptions [11,14,17].

The study has limitations that should be considered before publication. First, the formulation procedure contains a drug-amount discrepancy: the methods paragraph specifies 150 mg, whereas the formulation table specifies 200 mg for each batch. Second, the reported F3 24-h release is 95.56% in the Results section but 96.98% in the summary. Third, complete time-point release data and numerical release-kinetic statistics are needed to independently verify the selected kinetic model. Fourth, complete stability results were not available in the extracted source material. These issues should be resolved against the laboratory notebook and raw instrument outputs; they cannot be resolved from published literature.

Finally, this work reports in-vitro formulation and characterization. Although a sustained-release microsphere system may be investigated as a strategy to modify clopidogrel release, the present results do not demonstrate increased systemic bioavailability, improved clinical efficacy or reduced adverse effects. Published clopidogrel multiparticulate and gastroretentive studies provide formulation precedents, but their outcomes cannot be extrapolated to this formulation without direct comparative or pharmacokinetic evidence [3–5]. Future work should include full dissolution profiles, validated assay methods, stability-indicating analysis, batch reproducibility and in-vivo evaluation where scientifically justified.

5. CONCLUSION

Clopidogrel bisulphate-loaded HPMC microspheres were prepared by a solvent-extraction method and evaluated for physicochemical properties and in-vitro drug release. Increasing HPMC amount was associated with increased particle size, yield and encapsulation efficiency, while loading capacity decreased. F3 was selected in the source thesis on the basis of its reported 24-h release of 95.56%. The results indicate that HPMC amount is an important formulation variable for microsphere performance. Further verification of inconsistent source values, complete release-kinetic analysis, stability testing and in-vivo studies are required before making conclusions about bioavailability or clinical benefit.

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CONFLICT OF INTEREST

The author declares no conflict of interest.

DATA AVAILABILITY

The data reported in this manuscript are derived from the submitted dissertation. Additional raw experimental data should be made available by the author upon reasonable request, subject to institutional requirements.

REFERENCES

1. Rao KRK, Lakshmi KR. Design, development and evaluation of clopidogrel bisulfate floating tablets. *Int J Pharm Investig*. 2014;4(1):19–26. PMID: 24678458. <https://pubmed.ncbi.nlm.nih.gov/24678458/>
2. Tan C, Degim IT. Development of sustained release formulation of an antithrombotic drug and application of fuzzy logic. *Pharm Dev Technol*. 2012;17(2):242–250. doi:10.3109/10837450.2010.531739. PMID: 21062232. <https://pubmed.ncbi.nlm.nih.gov/21062232/>
3. Design and development of clopidogrel bisulfate gastroretentive osmotic formulation using quality by design tools. PMID: 28247292. <https://pubmed.ncbi.nlm.nih.gov/28247292/>
4. Development of novel high density gastroretentive multiparticulate pulsatile tablet of clopidogrel bisulfate using quality by design approach. *AAPS PharmSciTech*. 2017. doi:10.1208/s12249-017-0805-2. PMID: 28550603. <https://pubmed.ncbi.nlm.nih.gov/28550603/>
5. Preparation and characterization of clopidogrel bisulfate-hydroxypropyl- β -cyclodextrin mixed inclusion complex for improved intestinal solubility and anti-thrombotic efficacy. PMID: 35872021. <https://pubmed.ncbi.nlm.nih.gov/35872021/>
6. Freiberg S, Zhu XX. Polymer microspheres for controlled drug release. *Int J Pharm*. 2004;282(1–2):1–18. doi:10.1016/j.ijpharm.2004.04.013. PMID: 15336378. <https://pubmed.ncbi.nlm.nih.gov/15336378/>
7. Kim BK, Hwang SJ, Park JB, Park HJ. Preparation and characterization of drug-loaded polymethacrylate microspheres by an emulsion solvent evaporation method. *J Microencapsul*. 2002;19(6):811–822. doi:10.1080/0265204021000022770. PMID: 12569029. <https://pubmed.ncbi.nlm.nih.gov/12569029/>
8. Yang CY, Tsay SY, Tsiang RC. Encapsulating aspirin into a surfactant-free ethyl cellulose microsphere using non-toxic solvents by emulsion solvent-evaporation technique. *J Microencapsul*. 2001. doi:10.1080/026520401750063937. PMID: 11253939. <https://pubmed.ncbi.nlm.nih.gov/11253939/>
9. Preparation of microspheres of water-soluble pharmaceuticals. *J Microencapsul*. 1989;6(2):219–225. doi:10.3109/02652048909098024. PMID: 2723966. <https://pubmed.ncbi.nlm.nih.gov/2723966/>
10. Effect of various polymers concentrations on physicochemical properties of floating microspheres. PMID: 23798776. <https://pubmed.ncbi.nlm.nih.gov/23798776/>
11. Siepmann J, Peppas NA. Modeling of drug release from delivery systems based on hydroxypropyl methylcellulose (HPMC). *Adv Drug Deliv Rev*. 2001;48(2–3):139–157. doi:10.1016/S0169-409X(01)00112-0. PMID: 11369079. <https://pubmed.ncbi.nlm.nih.gov/11369079/>
12. Caraballo I. Factors affecting drug release from hydroxypropyl methylcellulose matrix systems in the light of classical and percolation theories. *Expert Opin Drug Deliv*. 2010;7(11):1291–1301. doi:10.1517/17425247.2010.528199. PMID: 20977292. <https://pubmed.ncbi.nlm.nih.gov/20977292/>
13. HPMC—A marvel polymer for pharmaceutical industry—patent review. *Recent Adv Drug Deliv Formul*. 2021;15(1):46–58. doi:10.2174/1872211314666210604120619. PMID: 34086557. <https://pubmed.ncbi.nlm.nih.gov/34086557/>
14. Release kinetics of hydroxypropyl methylcellulose governing drug release and hydrodynamic changes of matrix tablet. PMID: 34420504. <https://pubmed.ncbi.nlm.nih.gov/34420504/>
15. Levina M, Rajabi-Siahboomi AR. The influence of excipients on drug release from hydroxypropyl methylcellulose matrices. *J Pharm Sci*. 2004;93(11):2746–2754. doi:10.1002/jps.20181. PMID: 15389670. <https://pubmed.ncbi.nlm.nih.gov/15389670/>
16. The role of oral controlled release matrix tablets in drug delivery systems. PMID: 23678458. <https://pubmed.ncbi.nlm.nih.gov/23678458/>

17. Xu G, Sunada H. Influence of formulation change on drug release kinetics from hydroxypropylmethylcellulose matrix tablets. *Chem Pharm Bull (Tokyo)*. 1995;43(3):483–487. doi:10.1248/cpb.43.483. PMID: 7774032. <https://pubmed.ncbi.nlm.nih.gov/7774032/>
18. Understanding and managing the impact of HPMC variability on drug release from controlled release formulations. PMID: 24652662. <https://pubmed.ncbi.nlm.nih.gov/24652662/>
19. Park JB, Lim J, Kang CY, Lee BJ. Drug release-modulating mechanism of hydrophilic hydroxypropylmethylcellulose matrix tablets: distribution of atoms and carrier and texture analysis. PMID: 23855499. <https://pubmed.ncbi.nlm.nih.gov/23855499/>
20. Single emulsion-solvent evaporation technique and modifications for the preparation of pharmaceutical polymeric nanoparticles. PMID: 22734869. <https://pubmed.ncbi.nlm.nih.gov/22734869/>
21. Preparation and evaluation of Eudragit S 100 microspheres as pH-sensitive release preparations for piroxicam and theophylline using the emulsion-solvent evaporation method. PMID: 16754375. <https://pubmed.ncbi.nlm.nih.gov/16754375/>
22. Microspheres for controlled release drug delivery. PMID: 14680467. <https://pubmed.ncbi.nlm.nih.gov/14680467/>
23. An overview of the production methods for core-shell microspheres for parenteral controlled drug delivery. *Eur J Pharm Biopharm*. 2022. doi:10.1016/j.ejpb.2021.11.007. PMID: 34861359. <https://pubmed.ncbi.nlm.nih.gov/34861359/>
24. The parameters influencing the morphology of poly(ϵ -caprolactone) microspheres and the resulting release of encapsulated drugs. *Int J Pharm*. 2015. doi:10.1016/j.ijpharm.2015.07.068. PMID: 26235922. <https://pubmed.ncbi.nlm.nih.gov/26235922/>
25. The robustness and flexibility of an emulsion solvent evaporation method to prepare pH-responsive microparticles. *Int J Pharm*. 2009;377(1–2):135–141. doi:10.1016/j.ijpharm.2009.03.024. PMID: 19515519. <https://pubmed.ncbi.nlm.nih.gov/19515519/>