

Sustainable Public Health Policies for Improving Community Well-Being

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ABSTRACT

Social media has become an integral part of young people's lives, influencing communication, learning, and social interactions. This paper investigates both the positive and negative effects of social media on youth development. It explores educational opportunities such as collaborative learning, information sharing, and digital networking while also addressing concerns including cyberbullying, misinformation, screen addiction, and mental health issues. The study reviews empirical research to evaluate how responsible social media use can support academic achievement and civic participation. Findings suggest that digital literacy education and parental guidance play critical roles in maximizing benefits while minimizing risks. The paper recommends educational policies promoting responsible online behavior and critical thinking skills.

Keywords – Social Media, Youth Development, Digital Literacy, Education, Online Communication, Mental Health.

Figure 1:General Principles

I. INTRODUCTION

Arthritis is type of disease that refers to various types of joint conditions that causes inflammation in the joints. Osteoarthritis refers to a degenerative disease caused in the joints when the cartilage protecting the joint bone ends wear down overtime causing pain, stiffness and decreased mobility in spine, knees, hips and hands. The primary cause of this disease is due to genetics, obesity, injury and age-related wear. The common symptoms include joint pain, decreased range of motion, swelling, stiffness and grating sound during movement can occur. There are various stages of OA including minor asymptomatic cartilage changes to severe chronic bone-on-bone friction that causes a great deal of dysfunction and pain(1).The cases of OA ranges from 22% to 39% in India. The cases usually occur in women especially during post-menopausal period and in rural areas due to manual labor. The cases increase with age(2).The current treatment plan of OA majorly focuses on reducing discomfort from pain and improving function through lifestyle changes, medication and physical therapy. The non-pharmacological therapy includes weight loss to reduce joint stress, exercise to strengthen and physical therapy. Pain management treatment includes topical NSAIDs to minimize side effects, oral medications comprising of NSAIDs and acetaminophen, injections that provide temporary relief and Viscosupplementation may be used for knee OA. Surgery and radio frequency is used for severe cases(3).

Novel Drug Delivery Systems are controlled medication release technologies developed to improve efficacy and safety compared to standard dosage forms. Microspheres are a novel drug delivery system made up of biodegradable, natural, semi synthetic and synthetic polymers. The sizes of these particles range from 1µm to 1000µm. They are free flowing powders that yield site specific drug delivery, boost clinical outcomes and lower side effects. The structure of the microspheres warrants improved patient compliance, constant drug release and defends the drug from enzymatic breakdown, creating them appropriate for proteins(4–6). Microspheres offer several advantages in drug delivery systems. Reduction in particle size improves the solubility of drugs. Controlled release systems provide consistent and delayed drug discharge over an extended period. Improved bioavailability helps in maintaining steady plasma drug levels and enhances patient compliance. Reduced toxicity is achieved by minimizing the required dosage and decreasing adverse effects. Microspheres are useful in protein delivery because they protect drugs from enzymatic degradation. Ease of administration is improved as microspheres reduce dosing frequency and enhance patient convenience. Taste masking is possible by converting liquid drugs into solid forms, thereby masking bitter taste. Gastrointestinal protection is provided by coating, which prevents irritation of the GI tract. Biodegradable microspheres eliminate the need for surgical removal, making them suitable for non-surgical applications(7).

Microspheres also have certain limitations. Their production cost is high and less economical compared to conventional formulations. Polymer degradation may raise environmental sustainability concerns(8). Microsphere characterization involves evaluating parameters such as particle size, surface morphology, encapsulation efficiency, and drug release profile. Particle size influences drug release rate and encapsulation efficiency, and it can be measured using techniques like optical microscopy and laser diffraction. Surface morphology is examined using Scanning Electron Microscopy, which provides information about particle shape, porosity, and internal structure. Zeta potential assesses electrostatic interactions that affect syringeability and dispersion stability. Polymer properties and drug polymer interactions are analysed using techniques such as Gel Permeation Chromatography and Differential Scanning Calorimetry. In vitro drug release studies are performed under controlled conditions to evaluate drug release kinetics and to establish correlation with in vivo behaviour(9).

Azathioprine is a prodrug, which means it is activated by the body rather than being an active drug. This occurs in multiple stages. Initially, reductive cleavage of the thioether (-S-) converts it slowly and nearly entirely to 6-mercaptopurine (6-MP). This is mediated by glutathione and related molecules found in the intestinal wall, liver and RBCs without the need for enzymes. Similar to natural purines, 6MP is degraded to produce thioguanosine triphosphate (TGTP), thiooxyguanosine triphosphate (TdGTP), thioinosinemonophosphate (TIMP) and a number of other intermediates. A second route involves the methylation of 6-MP and TIMP's sulphur atom. The metabolic end products of AZA are thiouric acid (38%) and many methylated and hydroxylated purines, which are eliminated in the urine. The mechanism of action of AZA is that it inhibits purine synthesis. Purines are required to synthesize DNA and RNA. Inhibiting purine synthesis reduces DNA and RNA production, leading to immunosuppression.

Chitosan is a generally acknowledged non harmful material utilized in various formulations.

Chitosan has phenomenal potential for drug applications due to its biocompatibility, high charge thickness, prosperity, muco-adhesion, and infiltration improving effect over the regular surfaces. Chitosan shows its nontoxicity with alters drug release properties in novel plans in animals similarly as individuals with a LD50 of 16 g/kg in rodents. Chitosan can be quickly prepared either by lysozymes or by chitinases which can be conveyed by the conventional vegetation in

the human stomach related plot and exist in the blood. The research is aimed on formulating Azathioprine loaded microspheres using the emulsification – heat denaturation method to carry out sustained drug release, improved gastric residence time and enhanced bioavailability for effective treatment of OA(10,11).

The study presents a novel proposition of formulating Azathioprine as injectable microspheres to attain targeted and prolonged drug delivery, surpass its short half-life and poor bioavailability while decreasing the systemic toxicity and dose frequency compared to conventional drug delivery system.

II. MATERIALS AND METHODS

2.1 Materials – Azathioprine- Pfizer Healthcare India Pvt. Ltd. Sriperumbudur, Tamil Nadu 602117. Chitosan, liquid paraffin, tween-80, glutaraldehyde-Southern India Scientific Corporation, Kandhanchavadi, Chennai, Tamil Nadu 600096. Distilled water.

2.2 Pre-formulation studies

2.2.1 Organoleptic Properties – Azathioprine was studied for the properties like color and appearance(12).

2.2.2 Melting Point Determination – Azathioprine was finely powdered and filled in a capillary tube which was attached to a thermometer and placed in the melting point apparatus. It was gradually heated and the temperature at which the sample started to melt was noted(13).

2.2.3 Solubility Analysis – Solubility of Azathioprine was determined in solvents like distilled water, ethanol, methanol, phosphate buffer, etc. Small amount of drug in 10ml of solvent was shaken to make homogenous dispersions and kept at room temperature for 24 hours and observed for solubility and recorded(14,15).

2.2.4 Fourier Transformer Infrared Spectroscopy (FTIR) – Identification of the drug was carried out by using ATR-FTIR spectrophotometry. In this study, the drug and polymer reactions were checked. The main characteristic functional groups were determined in the fingerprint regions(16).

ATR-FTIR measurements were done for AZA, Chitosan and AZA_CHITOSAN_MS by Perkin Elmer Frontier, in the spectral wavelength ranging from 4000 cm⁻¹ to 400 cm⁻¹ at the resolution of 4 cm⁻¹. The baseline corrections were done using the software spectrum.

2.2.5 UV Spectroscopy–

2.2.5.1 Preparation of stock solution of AZA in Methanol and Scanning in UV–

UV Spectroscopy is concerned with the study of the absorption of UV-visible radiation. The wavelength at which maximum absorbance in the spectrum occurs is called λ_{max} . The analysis was done by measuring 276nm λ_{max} (17). Determination of λ_{max} of Azathioprine was done by UV Spectrophotometer Shimadzu 1800.

Procedure–10mg of AZA was placed in a 10ml of volumetric flask to which 5ml of methanol was added and the mixture was vortexed using a Cyclomixer (Remi) for 2 minutes. Methanol was added to increase to raise the volume to 10ml. This was the primary stock solution accounting for concentrations of 1000 μ g per ml. A diluted solution was scanned in a UV Spectrophotometer from 200-400 nm using methanol as blank.

2.2.5.2 Preparation of standard calibration curve of AZA in methanol –

From the above stock solution, dilutions were prepared using methanol to prepare solutions of concentrations ranging from 2, 4, 8, 10 and 12 micrograms per mL of AZA in methanol(18–20). The solutions were mixed using vortex mixture and the absorbance was measured at 276 nm (λ_{max}) using methanol as blank on Shimadzu 1800 UV-Visible Spectrophotometer and calibration curve was plotted. All the readings were taken in triplicate. The graph was plotted between absorbance and concentration (μ g/mL).

2.2.6 Compatibility Studies–

Medication polymer similarity study gives the system detailing of the dose structures and forecast

of the security of medication. Here medication – polymer similarity study is tried by utilizing FTIR and DSC study(21–26).

2.2.6.1 FTIR Study–The FTIR was performed for physical blend of medication and polymer.

2.2.6.2 DSC Study - The warm conduct of AZA unadulterated medication, chitosan polymer and AZA stacked Chitosan microsphere (AZA_CHITOSAN_MS) were concentrated via doing the DSC estimations utilizing a DSC1 instrument (Mettler Toledo, Switzerland)(27–31). Around 3mg of the sample was gauged and creased into the aluminium cauldrons. The temperature was kept at 30-400°C and the warming rate was kept up at 10°C/min.

2.3 Preparation of Azathioprine loaded in Chitosan microspheres–

AZA-loaded chitosan microspheres were created using the emulsification heat-denaturation process. Azathioprine (0.5 g) was dissolved in a 12.5 mL chitosan solution, and this aqueous phase was added dropwise into 50 mL liquid paraffin preheated to 60°C containing Tween 80 as an emulsifying agent(32–36). The mixture was stirred for 1 hour to allow microsphere formation, after which the temperature was reduced to 40 °C and maintained for 25 minutes for hardening. The microspheres were then stabilized by adding 25% v/v glutaraldehyde and stirring for 15 minutes. Microspheres were collected by decantation and rinsed with n-hexane to remove paraffin before drying at room temperature. The same procedure was followed for two batches using different concentrations of chitosan and Tween 80. The process is depicted in Figure 2 given below. The formulation were taken according to the Table 1.

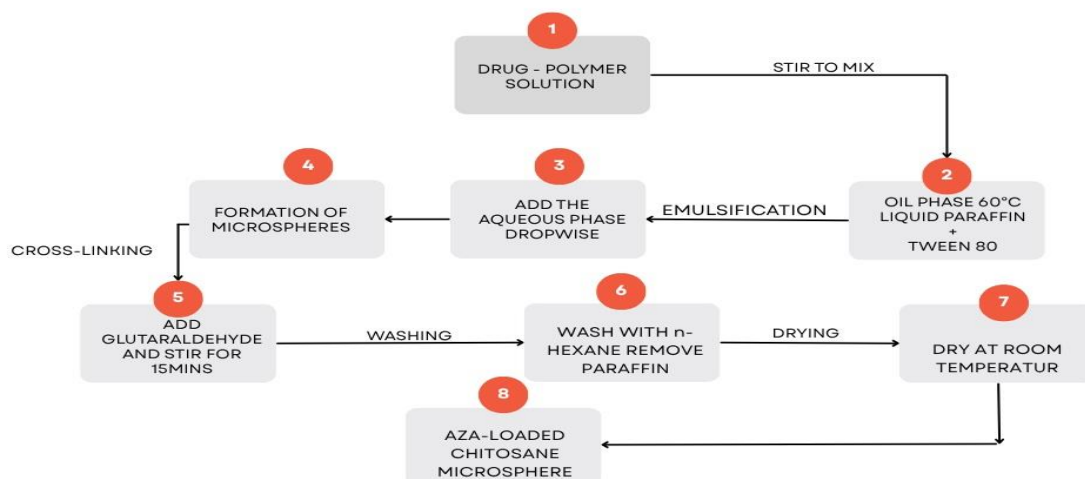


Figure 2: Preparation of Microspheres

Table1: Formulation table of Azathioprine microspheres

Formulation Code	Ingredients				
	AZA (mg)	Chitosan (mg)	Tween 80 (%)	Liquid paraffin (ml)	Distilled water (ml)
F1	100	100	1	50	100
F2	100	100	2	50	100
F3	100	100	4	50	100
F4	100	200	1	50	100
F5	100	200	2	50	100
F6	100	200	4	50	100

Glutaraldehyde was used as a cross-linking agent in all the formulations (F1-F6).

2.4 Characterization of prepared microspheres –

2.4.1 Zeta Potential –

The Zeta potential indicates that the azathioprine microspheres contain a negative surface charge that provides stability by inhibiting particle aggregation. The principal amount of charge provides acceptable electrostatic repulsion, aid good dispersion and physical stability of the microspheres.

2.4.2 In-vitro Drug Release Study –

The in-vitro drug release assesses the pace and the extent of release of microspheres. The device used in the investigation is USP Dissolution Apparatus II (paddle). Various dissolving mediums are utilised, including simulated stomach fluid and buffer with apH of 6.8. the microspheres are immersed in 900-1000ml of dissolving medium the temperature of the equipment is $37 \pm 0.5^\circ\text{C}$, and stirring speed is

50-75rpm. Samples are taken at regular intervals and replaced with fresh medium. The material is analysed using UV Spectroscopy at $\lambda_{\text{max}}=280\text{-}285\text{nm}$.

III. RESULTS

3.1 Organoleptic properties–AZA was observed to be pale yellow to yellow crystalline powder. The appearance coincided to the standard reference characteristics therefore confirming the identity and purity of the drug. No discolouration was observed that indicated the drug was suitable for further formulation.

3.2 Melting point determination–The melting point was observed to be 240°C , that within the range $238\text{--}245^\circ\text{C}$ for AZA. This confirms the authenticity of the drug sample. A melting point within the reported range denotes minimal impurities. The results were depicted in Table 2.

Table 2: Melting Point Determination

Melting point	Drug	Reported (°C)	Observed(°C)
1	Azathioprine	238–245 °C.	240°C.

3.3 Solubility analysis –The drug was observed to be insoluble in water but sparingly soluble in dilute alkali solutions and slightly soluble in ethanol. The solubility behaviour supports the need for controlled drug delivery.

3.4 FTIR –The FTIR spectra revealed the drug's unique function groups without noticeable peak

shifts. In the drug-polymer mixture, no new peaks or peak disappearances were noticed. This suggests that the medication and polymer are not chemically interacting. Compatibility was thus verified. The results were depicted in Figures 3 and 4.

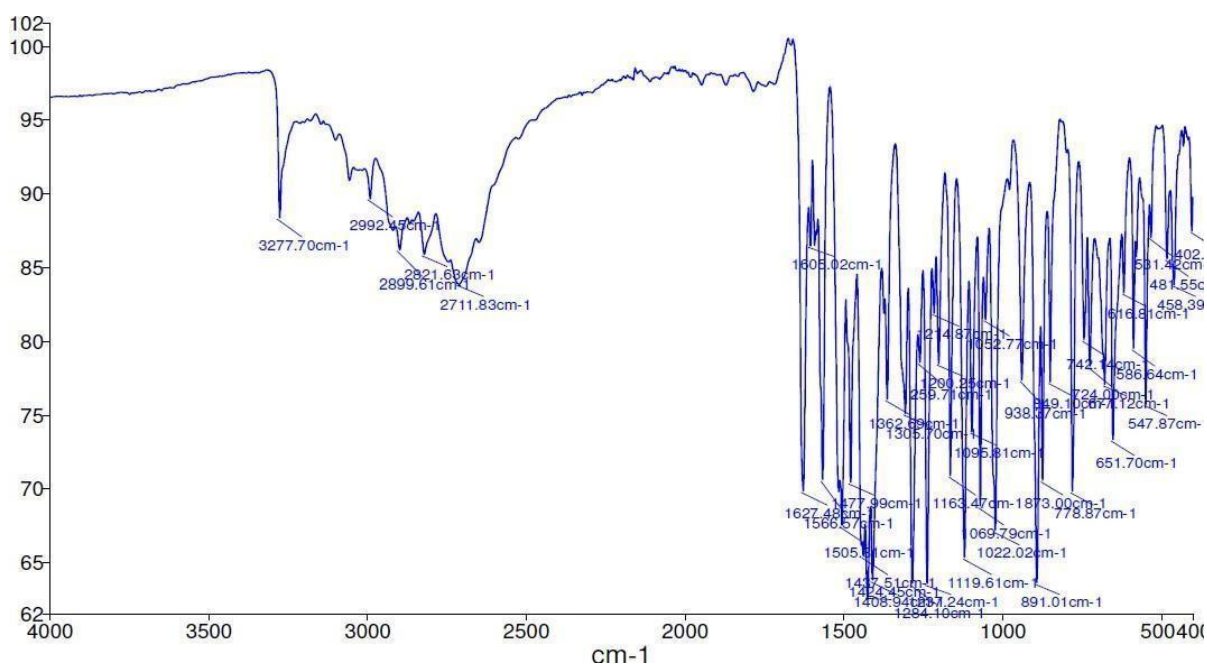


Figure 3: FTIR of Azathioprine

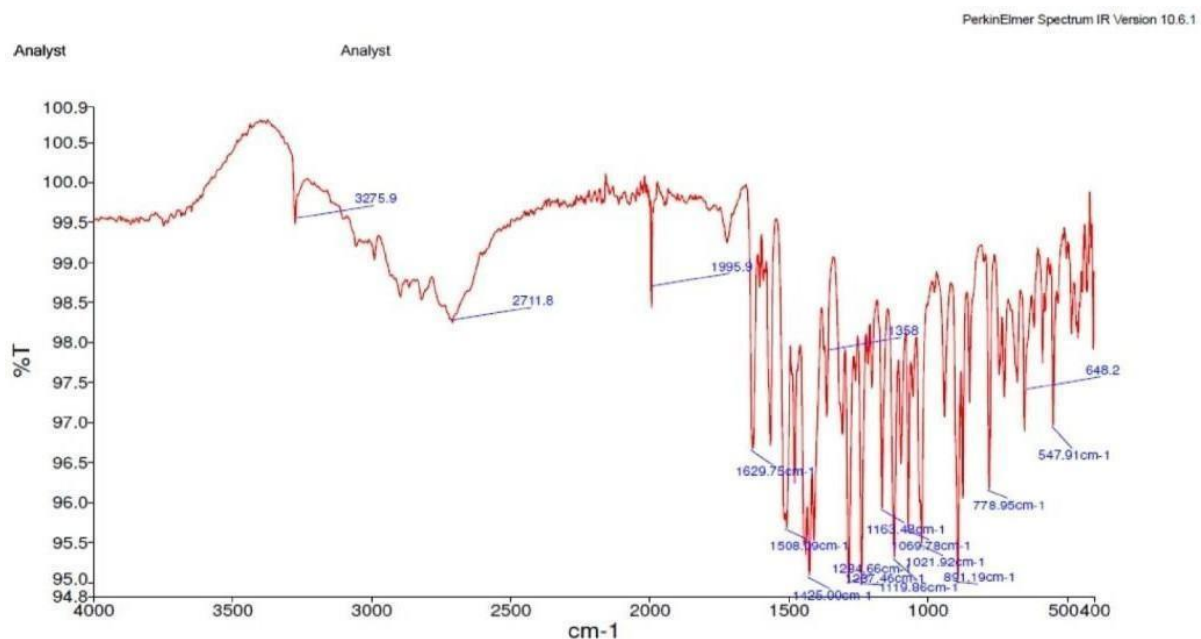


Figure 4: FTIR of Azathioprine and Excipients

3.5 UV Spectroscopy –At 276nm, the drug's absorbance peaked. The calibration curve indicated a strong linear relationship between absorbance and concentration. This attests to the accuracy and dependability of the analytical process. It was appropriate for additional research on medication

release and content. The graph was plotted between absorbance and concentration (µg/mL). Linear regression equation ($y = mx + c$) and coefficient of correlation (R^2) were used to analyse drug calibration curves in Figure 5 and tabulated in Table 3.

Table 3: Standard Calibration of Azathioprine in Methanol

Conc. (µg/mL)	Absorbance
0	0
2	0.165
4	0.326
8	0.503
10	0.648
12	0.801

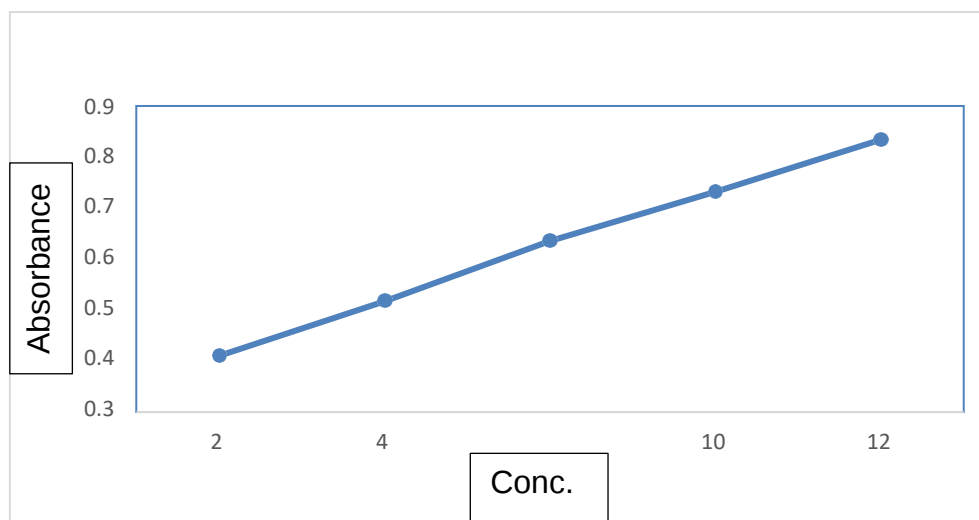


Figure 5: Calibration of Azathioprine

3.6 Compatibility Studies–

3.6.1 FTIR study–The FTIR spectra revealed the drug’s unique function groups without noticeable peak shifts. In the drug-polymer mixture, no new

peaks or peak disappearances were noticed. This suggests that the medication and polymer are not chemically interacting. Compatibility was thus verified. The results were depicted in Figure 6.

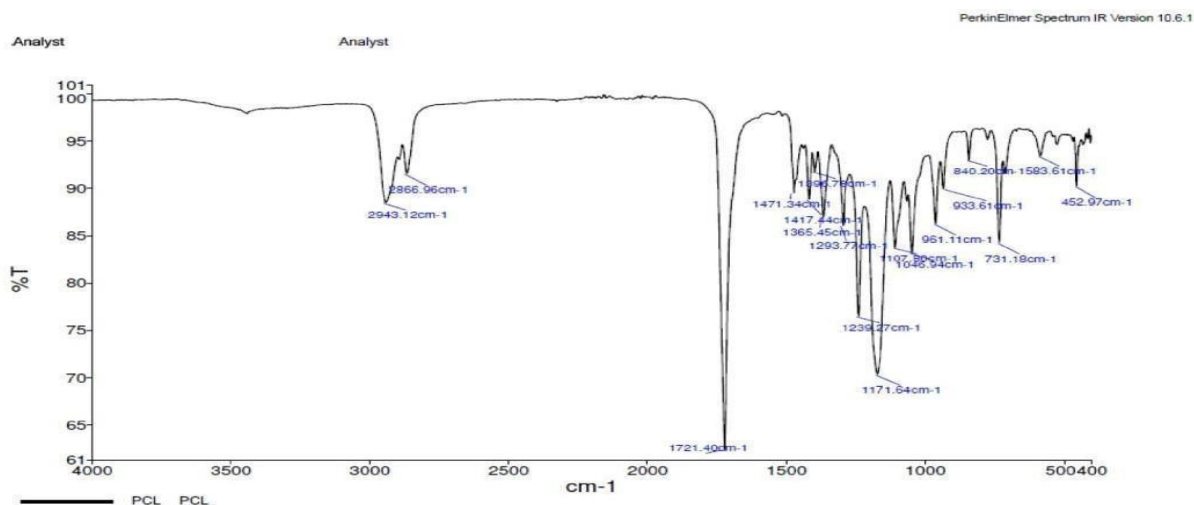


Figure 6: FTIR range of drug and polymer

3.6.2DSC Study–The drug’s melting point was represented by a distinctive endothermic peak on the DSC thermogram. Compatibility with the polymer is indicated by the formulation’s lack of

notable peak shifts. There was no discernible degradation. This attests to the formulation’s heat stability. The results are described in Figure 7.

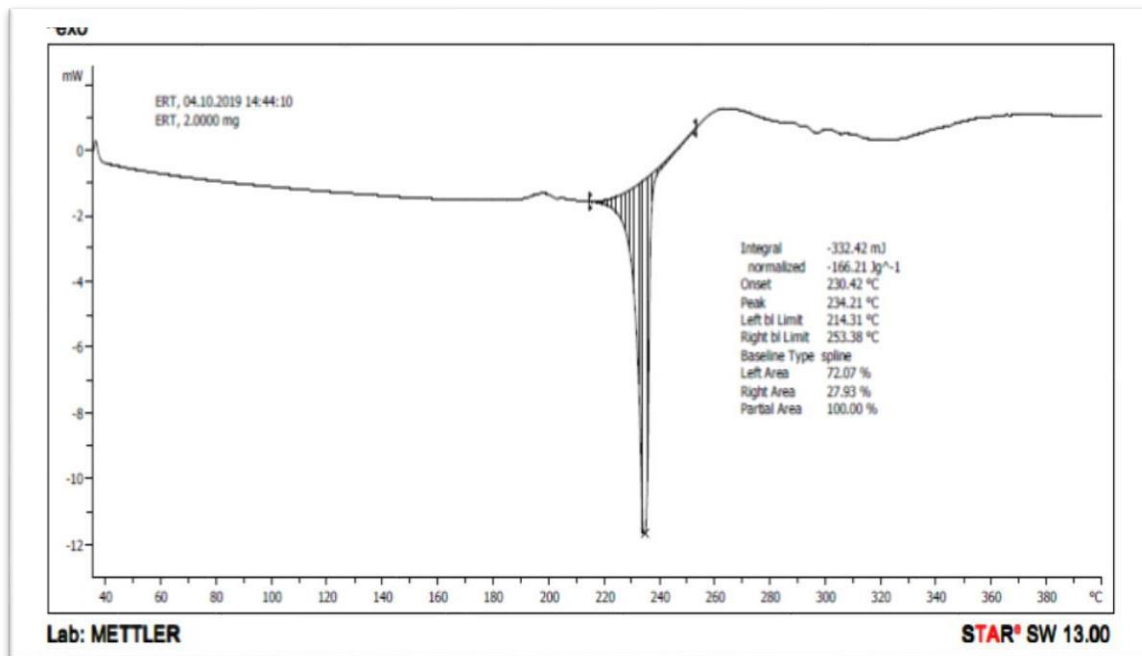


Figure 7 : DSC of Azathioprine

3.7 Characterization of prepared microspheres –
3.7.1 Zeta Potential –The zeta potential values of the microspheres were negative. Electrostatic repulsion between the particles is facilitated by this negative surface charge. It enhances physical stability and inhibits aggregation. Good dispersion stability is thus demonstrated by the formulation. The microspheres were discovered to be between 2 and 5 μm in size. Controlled preparation conditions are suggested by a uniform distribution of particle

sizes. Better control over drug release is facilitated by smaller particles sizes. The outcomes show that the microsphere formed successfully. The particle size was observed and depicted in Table 4. The cumulative frequency was found in Figure 8 and the particle size distribution in Figure 9. The zeta potential was found from Figure 10.

Table 4: Particle Size

Batch No.	Mean Molecule Size (μm) $\pm$ SD	Zeta Potential (mV)
FA1	3.68 $\pm$ 0.9	-11.03 $\pm$ 0.7
FA2	5.52 $\pm$ 1.2	-12.31 $\pm$ 0.6
FA3	3.22 $\pm$ 0.4	-13.81 $\pm$ 0.9
FA4	3.11 $\pm$ 0.4	-9.82 $\pm$ 0.4
FA5	5.32 $\pm$ 0.3	-10.54 $\pm$ 1.2
FA6	2.62 $\pm$ 0.2	-11.32 $\pm$ 0.6

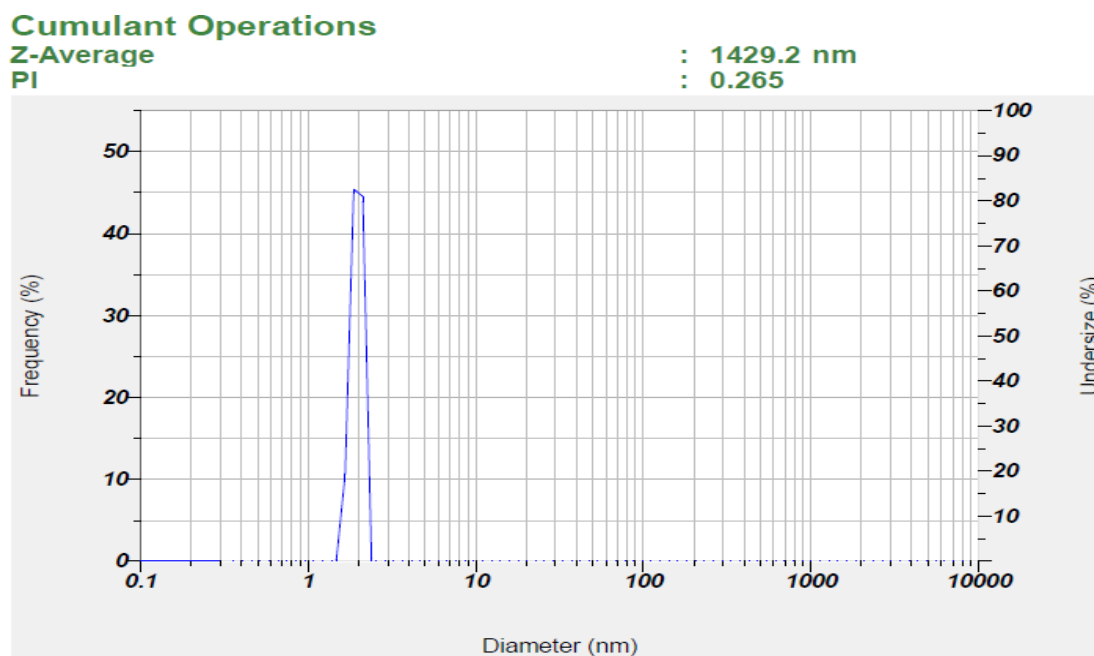


Figure 8: Cumulative Particle Size Distribution

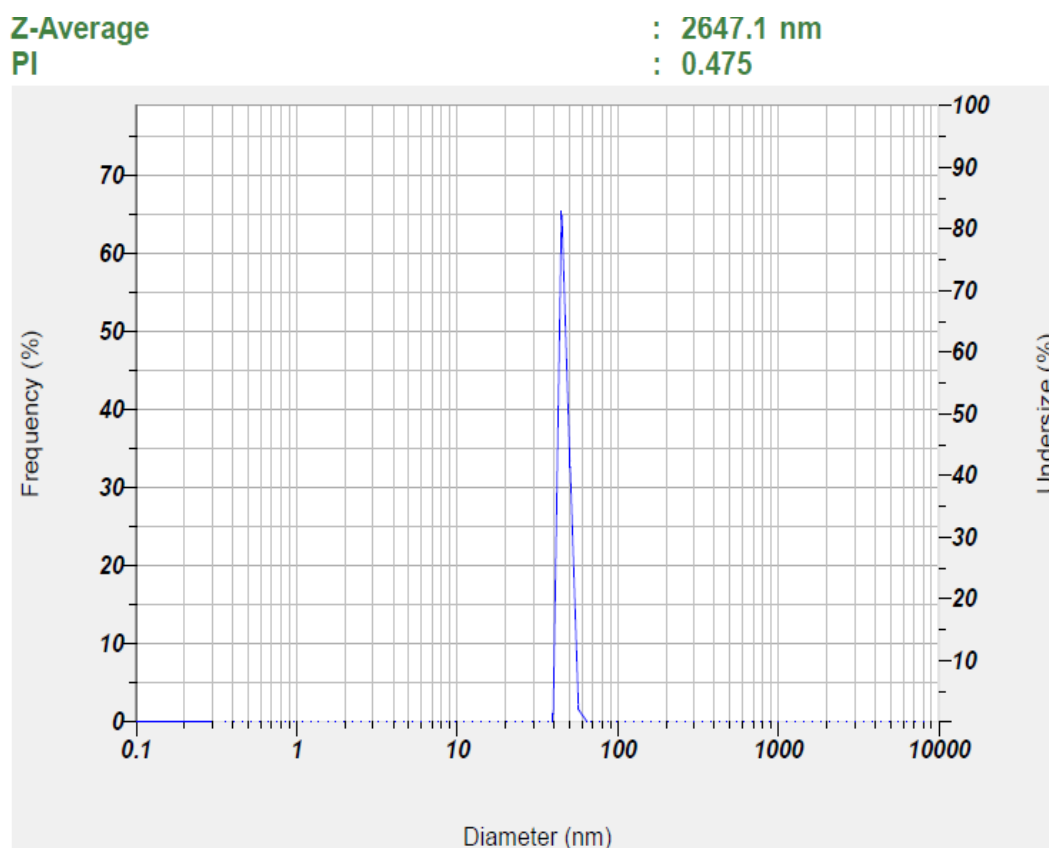


Figure 9: Particle Size Distribution

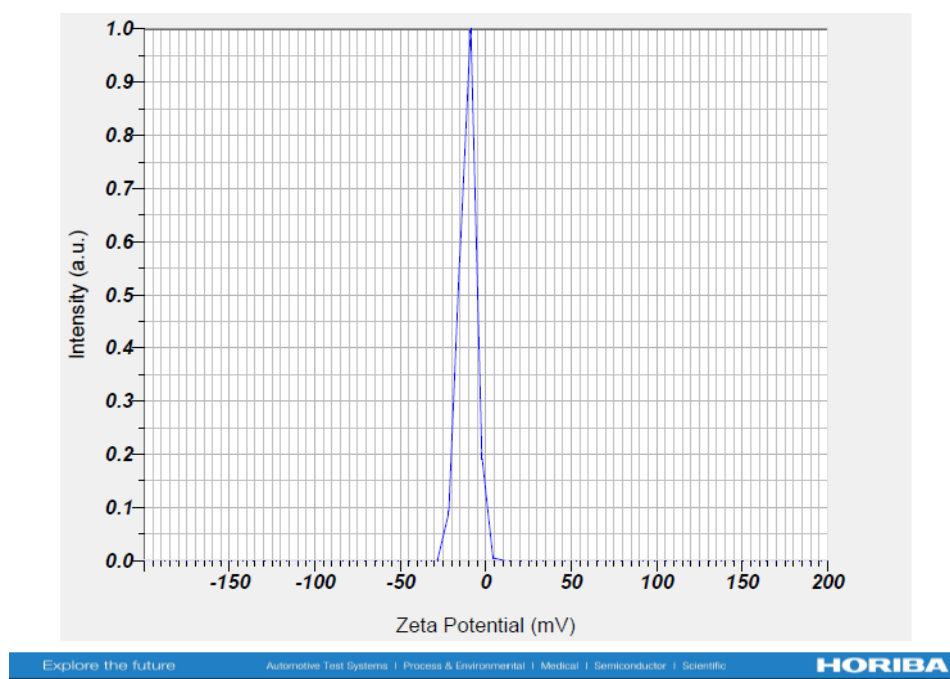


Figure 10: Zeta Potential of Optimized Formulation

3.7.2 In-vitro Drug Release Study – For up to 24 to 48 hours, the formulations demonstrated consistent drug release. Controlled diffusion-based release came after the initial burst release. This suggests persistent releasing behavior that has been

successful. The findings support microspheres' potential for long-lasting therapeutic benefit. The percentage release was tabulated in Table 5 and drug release study was found in Figure 11.

Table 5: In-vitro drug release study

Time (hrs.)	% Drug Release					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
0.5	32.5	28.5	28	21.3	11.83±2.3	22.43±1.8
1	52	42	48.7	42	24.22±2.7	36.9±4.1
2	65.3	55.3	61.3	55.3	29.23±1.5	52.23±2.5
4	78	68.7	75.5	68.7	40.65±1.9	62.76±2.1
6	87.3	82.1	85	82.1	54.16±2.0	78.77±3.5
12	98.8	88.8	97.5	88.8	62.52±2.7	85.18±3.2
24	-	99.1	-	98.2	79.05±4.5	99.7±0.1

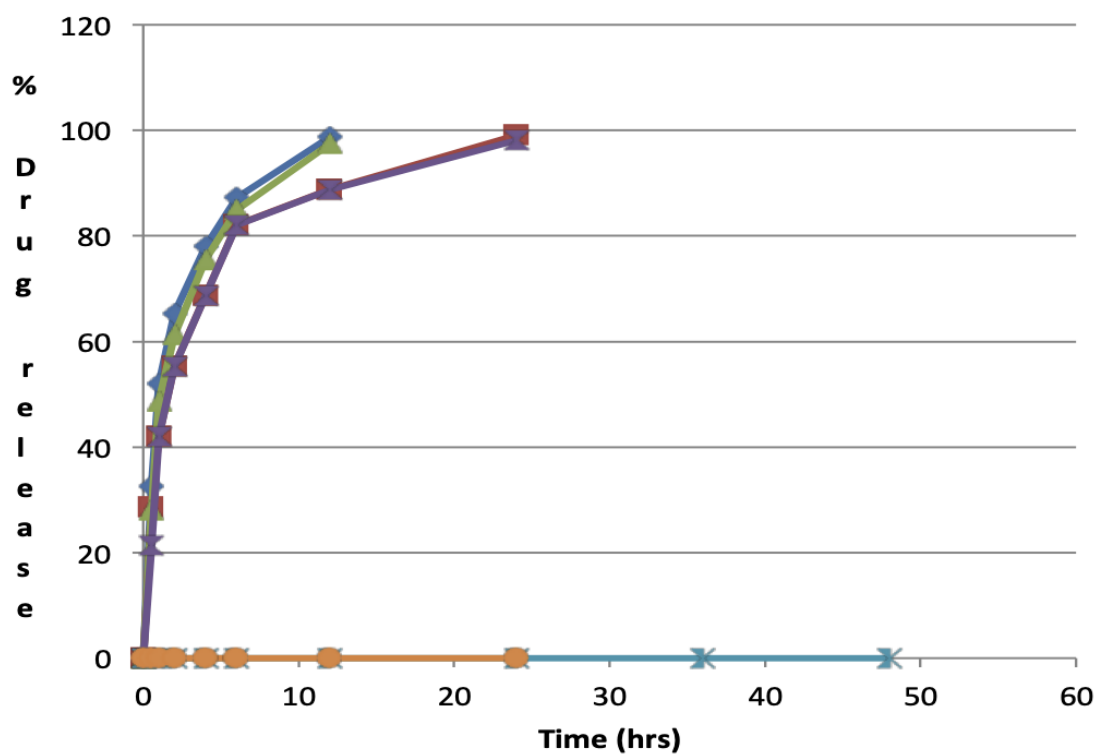
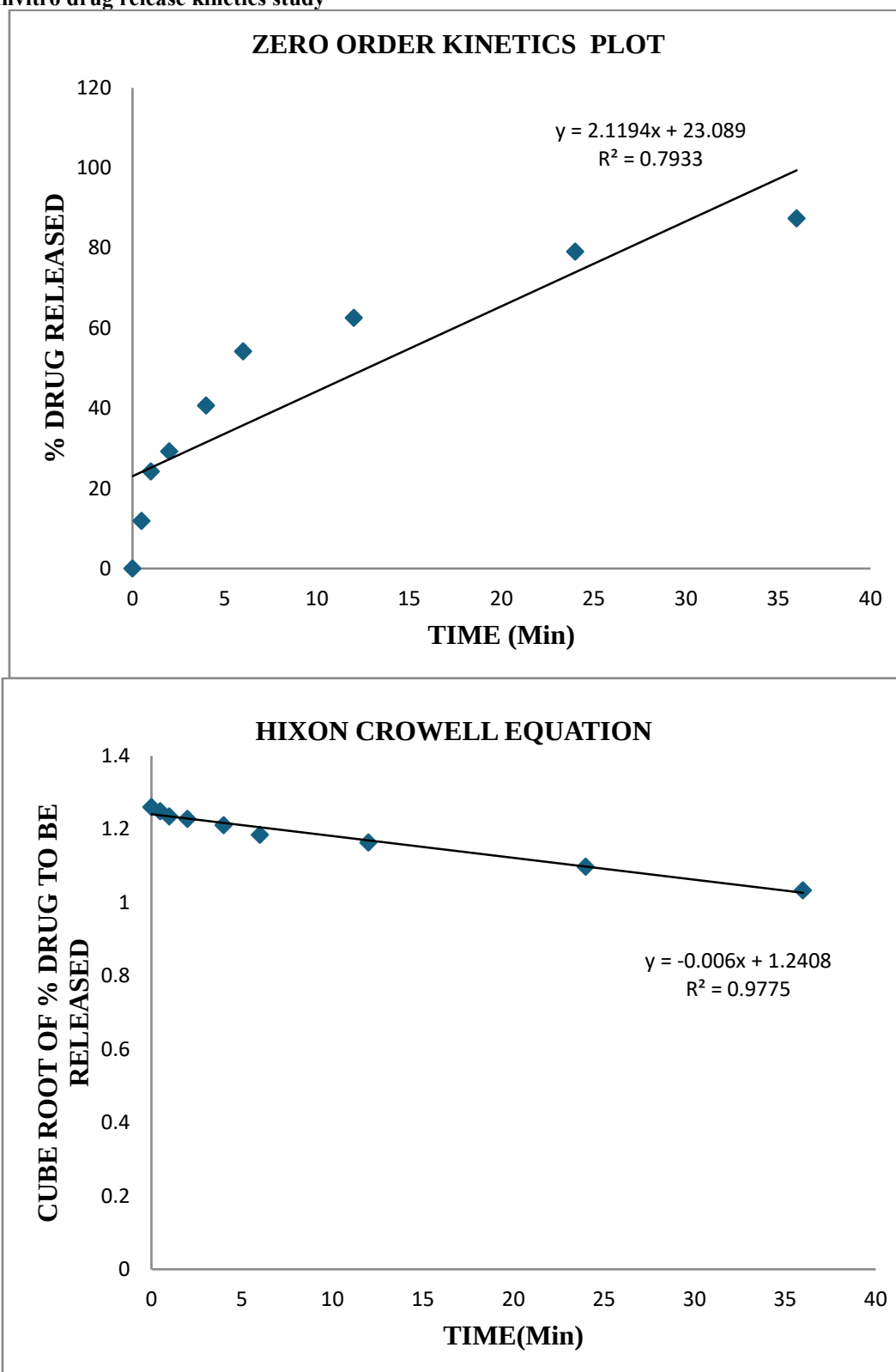


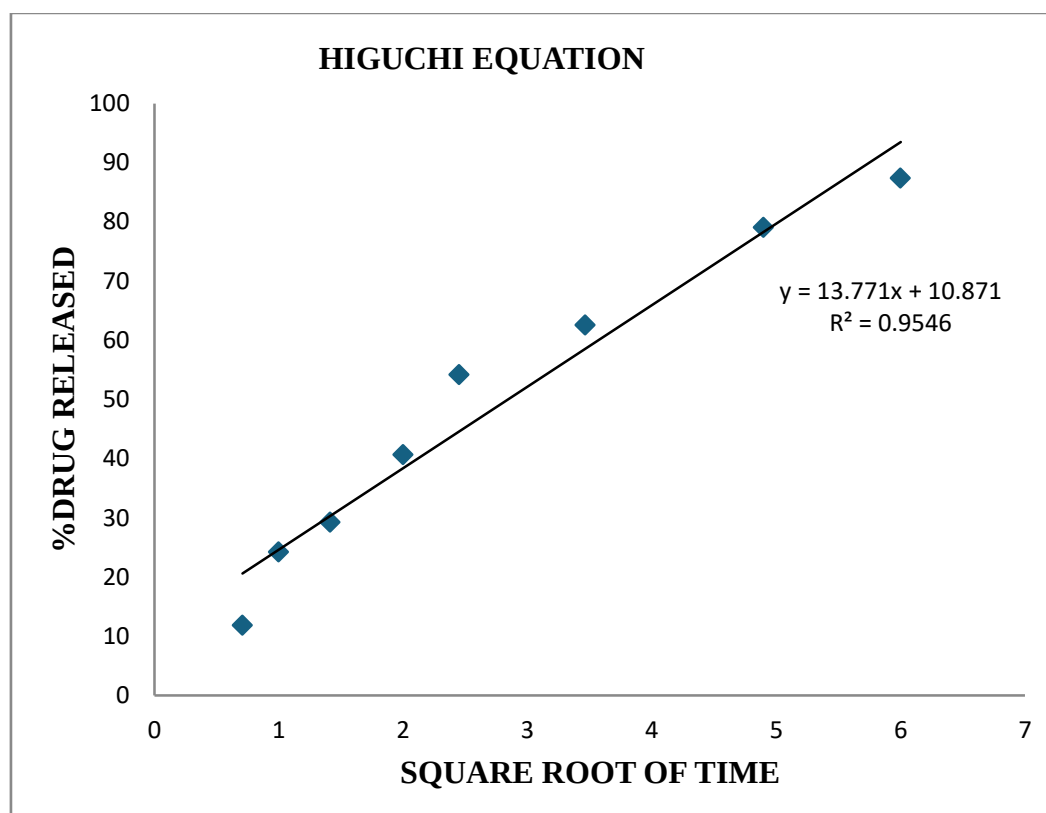
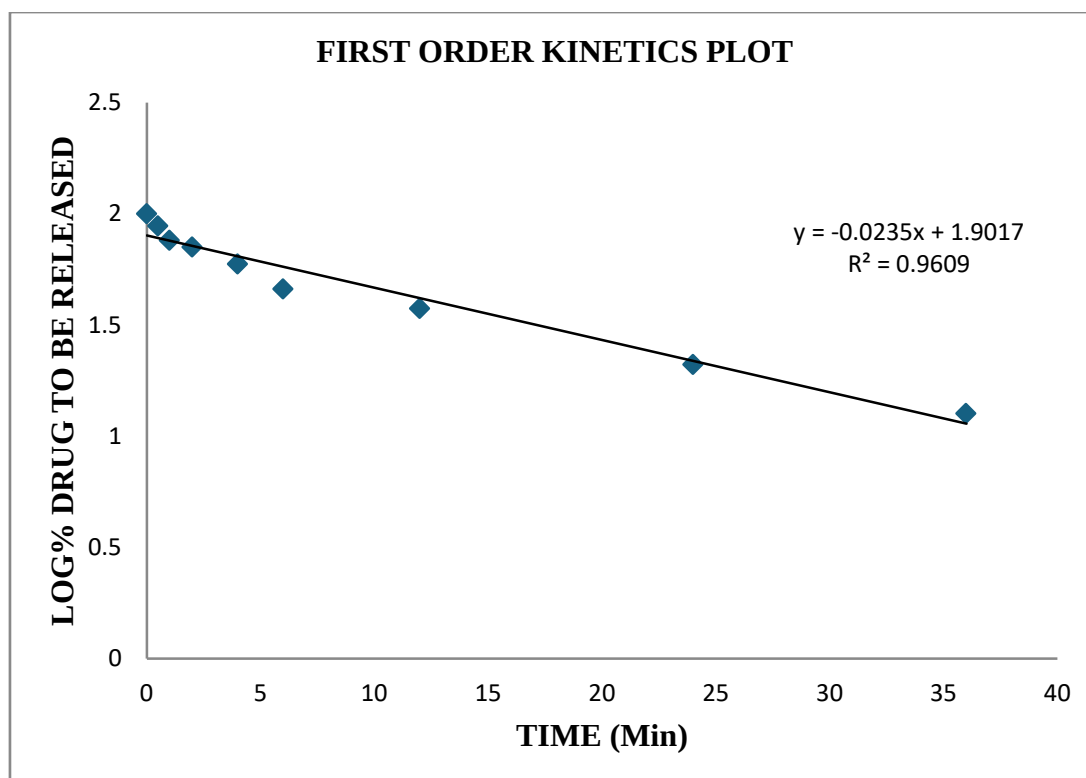
Figure 11: In vitro Drug Release of azathioprine microspheres

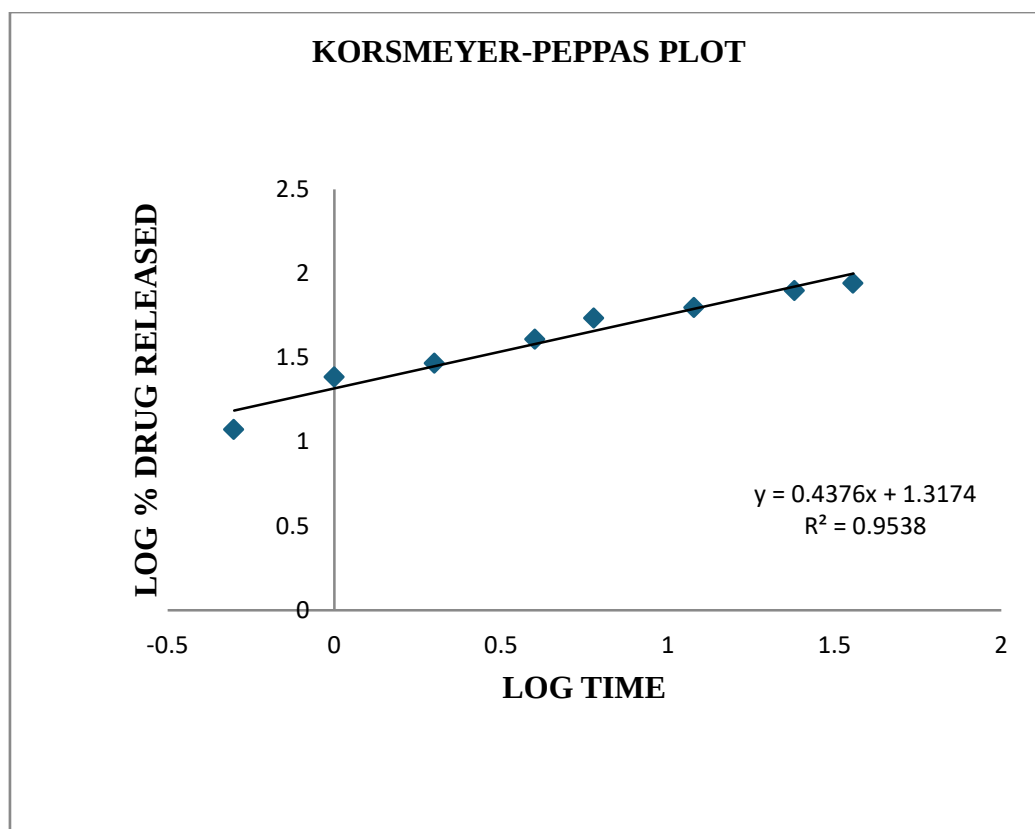
Formulation F6 was determined to be the best batch out of all the formulations (F1-F6) due to its improved sustained drug release profile (~95%

over 48 hours), acceptable zeta potential (-11.32 mV), and smallest particle size (2.62 μm).

3.7.3 Invitro drug release kinetics study







The drug release data were fitted into different kinetic models including zero-order, first-order, Higuchi, Hixson–Crowell, and Korsmeyer–Peppas models to determine the mechanism of drug release.

- Zero-order kinetics showed a moderate correlation ($R^2 = 0.7933$), indicating that drug release is not constant over time.
- First-order kinetics exhibited a high correlation ($R^2 = 0.9609$), suggesting that the drug release is concentration-dependent, where the release rate decreases over time.
- Higuchi model also demonstrated a strong fit ($R^2 = 0.9546$), indicating that the drug release follows a diffusion-controlled mechanism based on square root of time.
- Hixson–Crowell model showed the highest correlation ($R^2 = 0.9775$), suggesting that changes in surface area and particle size significantly influence drug release.
- Korsmeyer–Peppas model gave a good fit ($R^2 = 0.9538$) with release exponent ($n \approx 0.4376$), indicating a Fickian diffusion mechanism of drug release.

IV. DISCUSSION

In order to obtain sustained drug release and enhance therapeutic performance in OA, the current work sought to create microspheres containing azathioprine utilizing chitosan as a biodegradable

polymer.

This study's formulation strategy effectively created microspheres with the desired physicochemical characteristics. The lack of substantial interactions between the medication and polymer was confirmed by compatibility investigations using FTIR and DSC, suggesting that the drug's chemical integrity was unaffected by the formulation process. Maintaining medication stability and therapeutic efficacy depends on this.

Particle size analysis showed that the microspheres had a rather narrow distribution and were in micrometre range, indicating formulation uniformity. Because smaller particles have a higher surface area, which promotes quicker drug diffusion, the observed particle size is essential for regulating the drug release rate. Adequate electrostatic repulsion between particles was shown by the negative zeta potential values, which prevented aggregation and improved formulation stability(37–39).

A biphasic release pattern, defined by an initial burst release and a prolonged release phase, was shown by the in-vitro drug release investigations. Diffusion through the polymer matrix controls the following controlled release, whereas the medication on or near the microspheres' surface is responsible for the initial release. When hydrated, chitosan helps produce a gel-like barrier that controls the drug's dispersion into the surrounding

media.

Drug release was found to be delayed by an increase in polymer concentration, most likely as a result of the creation of a denser matrix structure that limits drug diffusion. This result emphasizes how crucial polymer concentration is as a formulation variable in regulating release kinetics(40–43).

Better fit to the Higuchi model revealed that the drug release primarily follows diffusion-controlled mechanisms, according to kinetic modelling of the release data. Formulation F6 was determined to be the optimal formulation based on the overall evaluation because of its balanced particle size, stability, and prolonged drug release. The appropriate polymer concentration, which enabled regulated drug diffusion over a prolonged period of time, may be responsible for the enhanced performance. Furthermore, the Korsmeyer-Peppas model revealed non-Fickian transport, indicating that drug release involves both polymer relaxation and diffusion pathways.

Compared to traditional dosage forms, the created microsphere system has a number of benefits, such as longer drug release, fewer doses, and better patient compliance. Such methods may improve overall treatment efficacy while reducing potential adverse effects related to peak drug concentrations by sustaining therapeutic drug level over an extended period of time(44).

Nevertheless, the study's scope is restricted to in-vitro assessment; additional in-vivo research is necessary to determine the formulation's pharmacokinetic and clinical performance. Future studies should also concentrate on investigating the viability of large-scale production and optimizing formulation variables.

Overall, the results show that the created microspheres are a viable drug delivery method for enhancing azathioprine's therapeutic efficacy in the treatment of OA(45,46).

Similar results have been documented in chitosan-based microspheres, where polymer concentration is crucial for regulating drug release and formulation stability. Additionally, the biodegradable and biocompatible characteristics of chitosan makes it a good carrier for sustained drug delivery applications(47–49).

V. CONCLUSION

The present study effectively generated azathioprine-loaded chitosan microspheres displaying sustained drug release over extended duration. The produced microspheres showed diffusion-controlled release behaviour and favourable physicochemical characteristics.

The optimized formulation F6 demonstrated stability, sustained drug release, and balanced

particle size, suggesting that it is appropriate for controlled drug administration. However, more in vivo research is needed to validate its therapeutic effectiveness.

DECLARATION

The authors declare no conflict of interest.

ABBREVIATIONS

OA - Osteoarthritis

SEM - Scanning Electron Microscopy

GPC - Gel Permeation Chromatography

DSC - Differential Scanning Calorimetry

ICH - International Council of Harmonisation

CHI - Chitosan

ATR-FTIR - Attenuated Total Reflectance-Fourier Transform Infrared Spectroscopy

AZA - Azathioprine

API - Active Pharmaceutical Ingredient

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not Applicable

CONSENT TO PUBLICATION

We give the consent to publish our research manuscript to the journal

AVAILABILITY OF DATA AND MATERIALS

The data was collected and calculated using the excel sheets

FUNDING

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AUTHORS

Patel Mahek Devangbhai- Conceptualisation, Validation, Investigation, Methodology, Formal analysis.

Soji Soman- Writing - Review & Editing, Visualization, Supervision.

Gayathri Hariharan-Writing-Original Draft, Conceptualization, Supervision, Project administration.

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