Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 32s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Formulation And Evaluation Of Gastroretentive Floating Microspheres And Bilayer Tablets Of Arbekacin And Gatifloxacin For The Treatment Of Urinary Tract Infections

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Cite this paper as: Nilam U. Metkari, Himmat Singh, Arehalli S. Manjappa, (2025) Formulation And Evaluation Of Gastroretentive Floating Microspheres And Bilayer Tablets Of Arbekacin And Gatifloxacin For The Treatment Of Urinary Tract Infections. *Journal of Neonatal Surgery*, 14 (32s), 7639-7648.

ABSTRACT

This study aimed to develop and evaluate gastroretentive bilayer tablets and floating microspheres containing Arbekacin and Gatifloxacin for the effective treatment of urinary tract infections (UTIs). Bilayer tablets were formulated with an immediate-release layer of Gatifloxacin and a sustained-release matrix of Arbekacin using HPMC and PEO polymers. Floating microspheres were prepared by emulsification solvent diffusion using polymer blends in varying ratios. Preformulation studies, drug-excipient compatibility (FTIR, DSC), and micromeritic properties were evaluated. In vitro drug release, buoyancy, swelling index, entrapment efficiency, and antimicrobial activity were assessed. Release kinetics were analyzed using Higuchi and Korsmeyer–Peppas models. The optimized bilayer tablets demonstrated rapid Gatifloxacin release (~90% in 45 minutes) and sustained Arbekacin release up to 14 hours. Microspheres provided a 24-hour controlled release profile with high entrapment efficiency (up to 89.4%) and buoyancy (94.6%). Drug release followed non-Fickian kinetics. Antimicrobial testing showed enhanced efficacy against *E. coli*, *K. pneumoniae*, and *S. aureus*. Stability studies confirmed formulation integrity over 90 days. The dual delivery system effectively combines immediate and sustained drug release, improves gastric retention, and demonstrates superior antibacterial activity. It offers a promising strategy for improving treatment outcomes in MDR-UTIs.

Keywords: *Antibacterial activity, Arbekacin, Bilayer tablets, Floating microspheres, Gatifloxacin, Urinary tract infections*

1. INTRODUCTION

Urinary tract infections (UTIs) represent one of the most prevalent categories of bacterial infections encountered in both community and healthcare settings. Globally, they affect approximately 150 million individuals each year, with a significantly higher prevalence among women due to anatomical and physiological predispositions. UTIs range from uncomplicated cystitis to severe conditions such as pyelonephritis and urosepsis, often necessitating prolonged antibiotic therapy (Morris et al., 2023; Hu et al., 2024).

The rising incidence of multidrug-resistant (MDR) uropathogens—such as *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Enterococcus faecalis*, and *Staphylococcus saprophyticus*—has rendered many conventional antibiotics ineffective, complicating treatment outcomes and increasing the economic and clinical burden on healthcare systems. MDR strains frequently possess resistance genes such as ESBLs (extended-spectrum β-lactamases) and AmpC β-lactamases, which can be horizontally transferred among bacterial species, leading to further spread of resistance (Aydın et al., 2020; Meena et al., 2021; Nejad et al., 2023).

Two promising antibiotics for the treatment of MDR UTIs are Arbekacin and Gatifloxacin. Arbekacin, an aminoglycoside derivative, is known for its strong bactericidal activity against methicillin-resistant *Staphylococcus aureus* (MRSA) and other Gram-positive cocci. Gatifloxacin, a fourth-generation fluoroquinolone, exhibits a broad spectrum of activity against Gram-

negative and Gram-positive pathogens by targeting DNA gyrase and topoisomerase IV. Despite their therapeutic potential, these agents face challenges such as poor gastrointestinal stability (Arbekacin) and reduced bioavailability under standard oral dosage due to rapid gastric emptying (Shimizu et al., 2021; Mattoo et al., 2021; Yang et al., 2021).

In this context, Gastroretentive Drug Delivery Systems (GRDDS) offer a viable solution. GRDDS are designed to prolong the gastric residence time of orally administered drugs, thereby enhancing their absorption window in the upper gastrointestinal tract. Among the various GRDDS approaches, floating drug delivery systems (FDDS)—including floating microspheres and tablets—have gained prominence due to their ability to remain buoyant in gastric fluids without affecting gastric motility. Microspheres, in particular, provide advantages such as controlled release, reduced dosing frequency, and minimized side effects, owing to their ability to maintain consistent plasma drug levels. On the other hand, bilayer tablets offer a platform to deliver two different drugs with distinct release profiles—an immediate-release layer to rapidly achieve therapeutic concentration and a sustained-release layer to maintain it over time (Bhalala et al., 2025; Ramadan et al., 2020).

Given the synergistic potential of combining Arbekacin and Gatifloxacin, the present study aims to formulate and evaluate both floating microspheres and bilayer tablets of these drugs using novel and conventional polymers. The overall goal is to improve bioavailability, gastric retention, and antimicrobial efficacy while reducing dosing frequency and enhancing patient compliance. The objective of this study was to develop and evaluate gastroretentive floating microspheres and bilayer tablet formulations of Arbekacin and Gatifloxacin using suitable polymers for the management of multidrug-resistant urinary tract infections.

2. MATERIALS AND METHODS

Materials

Arbekacin and Gatifloxacin were obtained as gift samples from certified pharmaceutical manufacturers. Formulation polymers included Polyethylene Oxide (PEO WSR 303, WSR N-60K), Hydroxypropyl Methylcellulose (HPMC K100M), and glyceryl behenate, chosen for their matrix-forming and release-sustaining properties. Natural bio adhesive polymers such as Neem gum, Damar gum, and Copal gum were also used. Standard excipients included microcrystalline cellulose (MCC), croscarmellose sodium, crospovidone, magnesium stearate, talc, and povidone K30. Methanol and acetonitrile (HPLC grade), potassium dihydrogen phosphate, and sodium borate buffer were used in analytical and dissolution procedures.

Preformulation and Compatibility Studies

Micromeritic Properties

Micromeritic properties such as bulk and tapped densities, Carr's index, Hausner ratio, and angle of repose were assessed to evaluate powder flowability and suitability for direct compression or granulation. These parameters guided process optimization for bilayer tablets and microspheres (Kumar Sahu et al., 2022; Kimishima et al., 2016).

Solubility Study

Solubility studies were conducted in solvents of varying polarity. Both drugs were freely soluble in acetic acid, lactic acid, and distilled water; moderately soluble in methanol, ethanol, DMSO, and DMF and poorly soluble in non-polar solvents like ether and chloroform (Table 1). These results informed solvent selection for formulation and analytical studies.

Table 1. Solubility Profile of Arbekacin and Gatifloxacin.

SN	Solvent	Solubility of Arbekacin	Solubility of Gatifloxacin
1	Acetone	Insoluble	Insoluble
2	Acetic acid	Freely soluble	Freely soluble
3	Benzene	Insoluble	Insoluble
4	Chloroform	Insoluble	Insoluble
5	Dichloromethane	Insoluble	Freely soluble
6	Dimethyl formamide	Soluble	Soluble
7	Dimethyl sulfoxide	Soluble	Soluble
8	Distilled water	Soluble	Soluble
9	Ethanol	Soluble	Soluble

10	Ether	Insoluble	Insoluble
11	Ethyl acetate	Insoluble	Freely soluble

Drug-Excipient Compatibility

Fourier Transform Infrared Spectroscopy (FTIR)

FTIR spectroscopy (4000–400 cm^{-1}) was employed to detect interactions between drug and excipients. No significant shifts or disappearance of functional group peaks were observed in physical mixtures, confirming compatibility.

Differential Scanning Calorimetry (DSC)

DSC analysis was conducted from 50–300°C (10°C/min) under nitrogen purge. Drug-polymer mixtures showed preserved melting transitions, indicating thermal stability and absence of major interactions.

Formulation of Bilayer Tablets

Bilayer tablets were designed for immediate Gatifloxacin release and sustained Arbekacin delivery. Granules were prepared using isopropyl alcohol as a binder, dried, and compressed into tablets (8 mm punch, 85 mg weight). Super disintegrants (Croscarmellose sodium, Crospovidone) enabled rapid Gatifloxacin release, while the sustained layer incorporated HPMC and PEO in varying ratios to modulate Arbekacin release kinetics (Kimishima et al., 2016; Chai et al., 2025).

Formulation of Floating Microspheres

Floating microspheres were prepared by emulsification solvent diffusion. A polymer-drug solution in ethanol–acetone was added dropwise to liquid paraffin containing 0.5% Span 80 and stirred at 800 rpm. After 4 hours, n-hexane was added to harden the microspheres, which were then filtered, washed with n-hexane, and air-dried. Formulations varied in drug-polymer ratios and types of polymers (glyceryl behenate, Neem gum, Damar gum, Copal gum).

Evaluation of Bilayer Tablets

Physicochemical properties

Physicochemical properties such as weight variation, thickness, diameter, hardness, and friability were within pharmacopeial limits.

Drug Content

Gatifloxacin content was determined via UV spectroscopy at 294 nm. Arbekacin content was analyzed using HPLC with o-phthalaldehyde (OPA) derivatization and detection at 330 nm with retention time of 7.5 minutes. All assays confirmed drug content within ±5% of the label claim (Albano et al., 2021; Gámez-Herrera et al., 2020).

Buoyancy Study

Buoyancy tests in 0.1 N HCl (pH 1.2) assessed floating lag time (FLT) and total floating time (TFT). Most formulations floated within 1 minute and remained buoyant for >12 hour. **Swelling Index**

Swelling studies measured weight gain over time, indicating matrix hydration and gel formation crucial for sustained release.

Evaluation of Floating Microspheres

Microspheres were assessed for particle size, yield, entrapment efficiency (EE), and buoyancy. Sizes ranged from 150–300 µm with uniform spherical morphology. Production yields were 70–85%. EE, determined via UV spectroscopy (207 nm), ranged from 65–90%, improving with higher polymer content. In vitro floatation in 0.1 N HCl at 37 ± 0.5 °C confirmed buoyancy for >12 hours, validating the microspheres' potential for prolonged gastric retention (Chechare & Siddaiah, 2024; Mora-Castaño et al., 2024; Khoshnood et al., 2023).

***In Vitro* Drug Release Studies**

Drug release was evaluated using USP Type I (basket) apparatus in 0.1 N HCl at 37 ± 0.5 °C. Gatifloxacin release was monitored at 294 nm using UV spectroscopy. Arbekacin release was quantified using HPLC following OPA derivatization. Sink conditions were maintained by replacing aliquots with fresh medium. Gatifloxacin exhibited rapid release (~90% in 45 minutes); Arbekacin showed prolonged release over 12–24 hours (Thoudoju et al., 2024).

Kinetic Modelling

Release kinetics were analyzed using zero-order, first-order, Higuchi, Hixson–Crowell, and Korsmeyer–Peppas models. Gatifloxacin followed first-order kinetics, indicating concentration-dependent release. Arbekacin release from both tablets and microspheres best fitted the Korsmeyer–Peppas model ($n \approx 0.51$), suggesting non-Fickian diffusion controlled by polymer matrix erosion and drug diffusion. Some formulations also aligned with the Higuchi model, highlighting diffusion-based release from hydrated matrices (Yadav et al., 2024).

Antimicrobial Activity

The antimicrobial activity of both dosage forms was tested against clinical isolates of *Escherichia coli*, *Klebsiella pneumoniae*, and *Staphylococcus aureus* using the agar well diffusion method. Bacterial cultures were standardized to 0.5 McFarland turbidity, inoculated on Mueller–Hinton agar plates, and treated with 100 µL of sample solutions. Standard drug solutions were used as controls. Plates were incubated at 37 ± 1 °C for 24 hour, and zones of inhibition were measured. Both formulations showed strong inhibitory effects, with zone diameters comparable or superior to those of pure drugs. The bilayer tablets and microspheres demonstrated enhanced efficacy, likely due to the synergistic and sustained action of Gatifloxacin and Arbekacin. These results support their potential in managing UTIs effectively (Urnukhsaikhan et al., 2021; Bakadia et al., 2022).

Stability Analysis

Stability studies were conducted for optimized bilayer tablets and floating microspheres as per ICH Q1A(R2) guidelines under accelerated (40 ± 2 °C / 75 ± 5 % RH) and ambient (25 ± 2 °C / 60 ± 5 % RH) conditions over 90 days. Samples were evaluated at 0, 30, 60, and 90 days for physical integrity, drug content, buoyancy, and in vitro release. Gatifloxacin and Arbekacin content were determined using UV spectrophotometry and HPLC (OPA derivatization), respectively. Floating lag time and duration were assessed in 0.1 N HCl, and release profiles were analyzed using USP Type I dissolution apparatus. Similarity factor (f2) analysis confirmed no significant changes (f2 > 50), and drug content remained within acceptable limits (90–110 %), indicating good formulation stability (Arumugam et al., 2021).

Statistical Analysis

All experiments were conducted in triplicate (n = 3), and results are presented as mean ± SD. Statistical comparisons between formulations were performed using one-way ANOVA. A significance level of $p < 0.05$ was considered statistically meaningful. Kinetic model fits were evaluated based on regression coefficients (R^2 values).

3. RESULTS

Preformulation and Compatibility Studies

Micromeritic evaluation confirmed good flowability for both APIs and excipients, with Hausner ratios <1.25 and Carr's indices <20 %. Solubility studies revealed limited aqueous solubility for both drugs, justifying the need for sustained-release and gastroretentive systems.

FTIR, DSC, and TGA Analysis

FTIR spectra confirmed the integrity of functional groups with no significant peak shifts, suggesting drug–excipient compatibility (Figure 1). DSC of pure drugs showed a sharp endothermic peak at 305°C, while the optimized formulation displayed altered but stable transitions at 271°C and 404°C, indicating polymer interaction without new compound formation. TGA supported these findings, showing controlled degradation in the optimized formulation, suggesting improved thermal stability (Figure 2A and B).

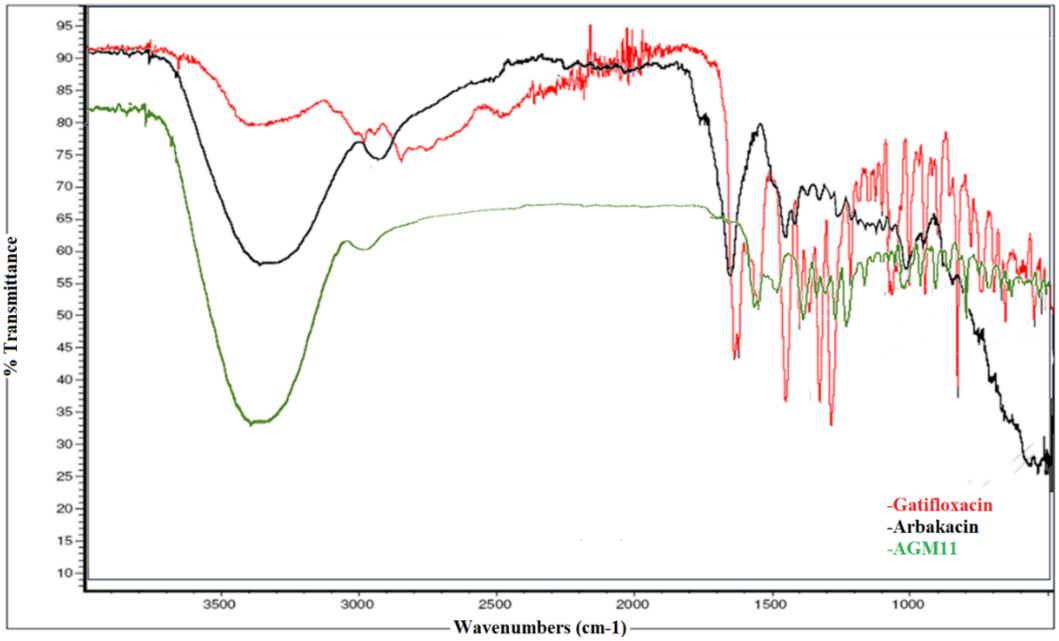

Figure 1. FTIR Spectra for drug excipient compatibility studies.

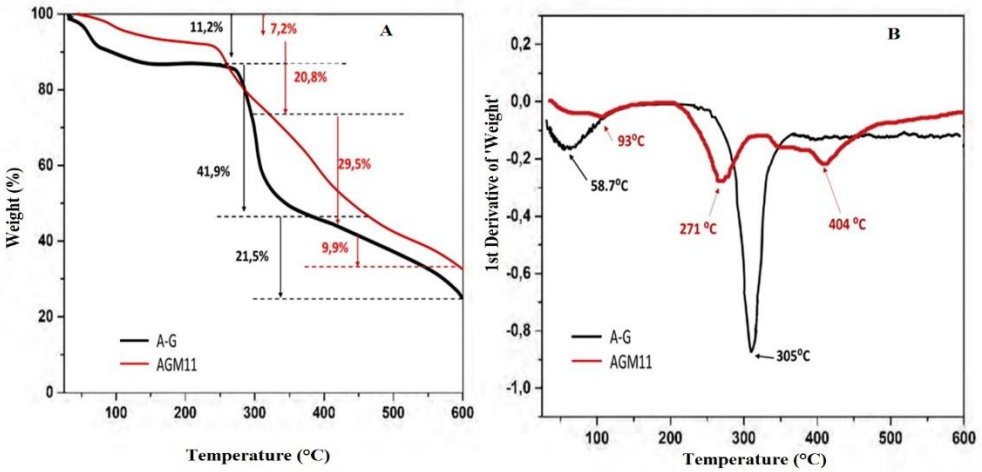

Figure 2. TGA thermogram of pure drugs and AGM11 (A) graph of the first-order derivatives of the weight loss of Pure drug and AGM11 (B).

Evaluation of Bilayer Tablets

Tablets passed pharmacopeial standards, with consistent weight, hardness (4.2–4.5 kg/cm²), and friability (<0.7%). Thickness averaged 2.6 ± 0.1 mm, and uniformity of dosage was confirmed.

Drug Content (Assay) Analysis

The immediate-release Gatifloxacin layer showed 97.8 ± 0.9% drug content using a UV-visible method ($R^2 = 0.9994$) (Figure 3). The Arbekacin sustained-release layer showed 98.3 ± 1.1% using HPLC with OPA derivatization. Assay data confirmed uniform drug distribution and reliable formulation performance.

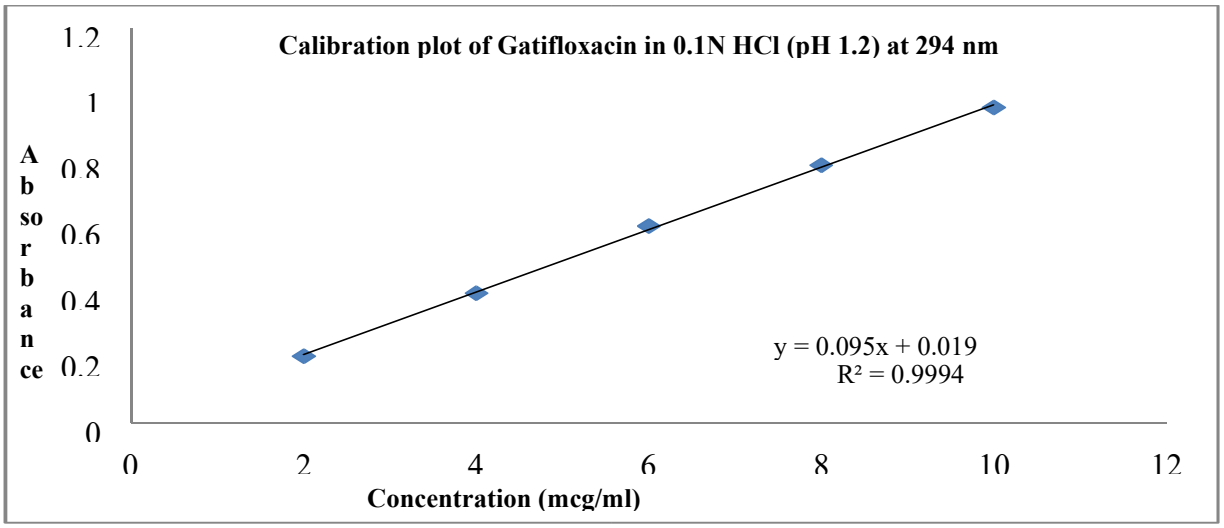

Figure 3. Calibration plot of Gatifloxacin in 0.1N HCl (pH 1.2) at 207 nm.

Buoyancy and Swelling

The optimized bilayer tablets floated within 56 ± 7 second and remained buoyant for over 12 hour. Swelling studies showed progressive weight gain over 6 hours, indicating effective matrix hydration and gel barrier formation—essential for sustained drug release.

Evaluation of Floating Microspheres

Microspheres demonstrated high yield (84–91 %) and optimal particle size (90–130 µm), suitable for gastric retention. They remained buoyant >12 hours, as visualized in simulated gastric fluid (Figure 4). The architecture supported sustained release and low density essential for gastroretention.

Figure 4. Determination of floating lag time and total floating time of the formulations prepared.

Entrapment Efficiency

Entrapment efficiencies ranged from 76.5–88.2 % (Gatifloxacin) and 80.3–89.4 % (Arbekacin). Formulation PM4 with PEO WSR 303 + PEO N-60K showed the highest efficiency. Optimized formulations showed >94 % buoyancy efficiency.

Micromeritic Properties of API and Excipients

Most excipients showed good flow (C.I. <25%, Hausner Ratio <1.35). Natural gums like Neem and Copal were particularly effective. However, excipients like Magnesium Stearate exhibited poor flow (C.I. >40%), requiring careful blending. These insights guided rational excipient selection.

***In Vitro* Drug Release and Kinetics**

Bilayer tablets demonstrated a biphasic release profile: Gatifloxacin released 90% within 45 minutes, while Arbekacin released over 12–14 hour. While, microspheres exhibited sustained release for 24 hours, with an initial burst followed by prolonged diffusion and erosion-controlled release.

Release kinetics

Release kinetics best fit the Higuchi model ($R^2 > 0.99$), indicating diffusion-dominated mechanisms. Korsmeyer–Peppas analysis showed anomalous transport ($n = 0.45–0.89$), confirming combined diffusion and erosion processes. The prolonged release profile supports reduced dosing frequency and sustained therapeutic levels.

Zero-Order

- k=5.43
- Linear release over time (less accurate for matrix systems)

First-Order

- k=0.138
- Concentration-dependent release

Higuchi Model

- k=21.92
- Best fits diffusion-controlled release from a hydrated matrix

Korsmeyer–Peppas Model

- k=21.53
- Non-Fickian diffusion ($0.45 < n < 0.89$), suggesting a combination of diffusion and erosion mechanisms

Arbekacin shows a sustained release profile, gradually reaching 97% over 24 hours. Gatifloxacin demonstrates immediate release, reaching 88–90% within the first hour and plateauing thereafter.

Stability Studies

Stability testing over 90 days under ICH Q1A (R2) conditions (25 ± 2 °C/60 ± 5% RH and 40 ± 2 °C/75 ± 5% RH) revealed no significant changes in color, integrity, or drug content (within 90–110%). Buoyancy and drug release profiles remained consistent ($f2 > 50$), confirming physical and chemical stability (Table 2).

Table 2. Stability study of formulation for 90 days.

Parameter	Initial (0 Days)	30 Days	60 Days	90 Days	Acceptance Criteria
Appearance	No change	No change	No change	No change	No significant change
Gatifloxacin content (%)	97.8 ± 0.9	97.5 ± 1.1	97.2 ± 1.0	96.9 ± 1.3	95–105% of label claim
Arbekacin content (%)	98.3 ± 1.1	98.0 ± 1.2	97.7 ± 1.0	97.3 ± 1.4	95–105% of label claim
Floating Lag Time (s)	56 ± 7	58 ± 6	57 ± 5	59 ± 6	≤ 2 min acceptable
Total Floating Time (h)	>12	>12	>12	>12	≥ 12 hours
% Drug release (GAT, 45 min)	~90%	~89%	~89%	~88%	Not <85% within 45 minutes
% Drug release (ARB, 12 h)	~90%	~89%	~88%	~88%	Sustained up to 12 h
Similarity factor (f2)	—	72.1	68.5	65.7	f2 > 50 = Similar profile

Antimicrobial Activity

The antimicrobial efficacy of the optimized bilayer tablets and microspheres was evaluated against clinical isolates of *E. coli*, *K. pneumoniae*, and *S. aureus* (including MRSA). Antibacterial assays demonstrated that bilayer tablets and microspheres retained and enhanced the antimicrobial efficacy of Arbekacin and Gatifloxacin. Agar well diffusion results showed inhibition zones comparable to or larger than standard solutions (Figure 5).

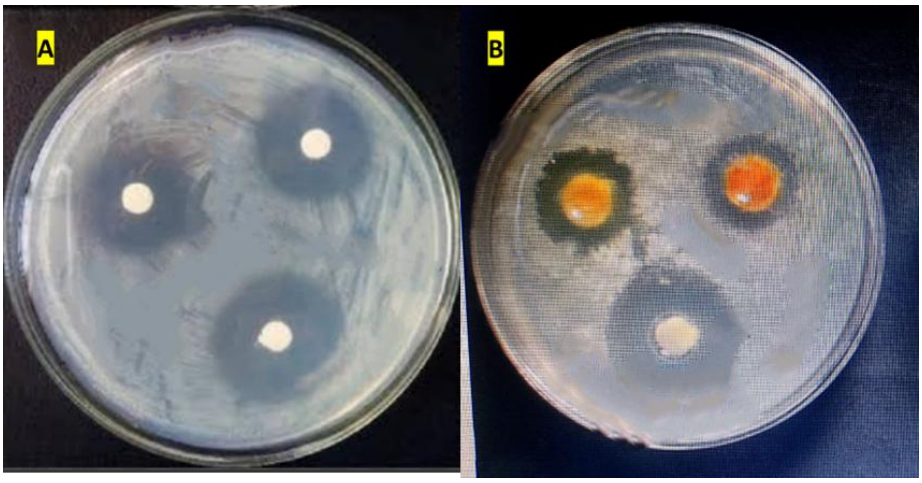

Figure 5. A) Zone of Inhibition by pure drugs (Arbekacin and Gatifloxacin) showing moderate antibacterial activity; B) Zone of Inhibition by optimized formulation (AGM11) showing enhanced antibacterial efficacy with notable clarity and diffusion zone.

The antimicrobial activity of the prepared formulations was evaluated against Escherichia coli, Klebsiella pneumoniae, and Staphylococcus aureus (including MRSA) using the agar diffusion method. The data revealed that all formulations exhibited varying degrees of inhibitory activity, confirming their potential efficacy against multidrug-resistant uropathogens.

Against *E. coli*, the formulation AGM7 demonstrated the highest mean zone of inhibition (19.00 ± 0.25 mm), followed closely by AGM4 (17.00 ± 0.35 mm), AGM8 (16.00 ± 0.20 mm), and AGM12 (16.00 ± 0.17 mm). These formulations significantly outperformed others, suggesting better drug release kinetics and enhanced antimicrobial penetration. For *K. pneumoniae*, AGM7 again showed superior activity with a mean zone of 18.50 ± 0.25 mm, followed by AGM4 (16.50 ±

0.25 mm), AGM12 (16.00 ± 0.25 mm), and AGM8 (15.50 ± 0.25 mm). The observed trend was consistent with the results against E. coli, reinforcing the robustness of these formulations. In the case of *S. aureus*, the largest inhibition zone was observed for AGM7 (18.00 ± 0.20 mm), with AGM4 (16.00 ± 0.20 mm), AGM8 (15.50 ± 0.30 mm), and AGM12 (15.00 ± 0.20 mm) following closely (Table 3). The consistent performance across all three pathogens indicated a broad-spectrum antibacterial effect of the optimized formulations.

Table 3. Zone of inhibition (mean ± SD) of formulated dosage forms against *E. coli*, *K. pneumoniae*, and *S. aureus.*

Formulation Code	ZOI		
	E. coli	***K. pneumoniae***	***S. aureus***
AGM1	10 ± 0.98	16 ± 0.79	11± 1.49
AGM2	10 ± 0.89	8 ± 1.13	18 ± 1.02
AGM3	14 ± 0.84	15 ± 0.59	8 ± 1.11
AGM4	9 ± 1.23	17 ± 0.93	14 ± 0.62
AGM5	11 ± 0.94	11 ± 0.93	12 ± 1.33
AGM6	18 ± 0.56	12 ± 0.99	15 ± 1.1
AGM7	19 ± 0.9	14 ± 0.93	19 ± 1.05
AGM8	17 ± 1.24	9 ± 0.81	14 ± 0.84
AGM9	14 ± 0.68	13 ± 0.93	15 ± 0.8
AGM10	9 ± 0.68	14 ± 1.39	9 ± 0.92
AGM11	8 ± 1.03	19 ± 1.44	19 ± 1.18
AGM12	9 ± 1.03	10 ± 1.0	18 ± 1.38

4. DISCUSSION

This study successfully formulated gastroretentive bilayer tablets and floating microspheres of Arbekacin and Gatifloxacin to address multidrug-resistant urinary tract infections (MDR-UTIs). The preformulation data confirmed good flow properties of the APIs and excipients, while FTIR and DSC analyses showed no significant drug–excipient interactions, supporting formulation stability.

The derived micromeritic properties of the drug and key excipients were evaluated in terms of bulk density (BD), tapped density (TD), compressibility index (C.I.), Hausner ratio (HR), and angle of repose (AR). Among the drugs, Arbekacin and Gatifloxacin exhibited good flow properties with C.I. values of 26.09% and 25.53%, respectively, and HR values below 1.36. Polymeric excipients such as Polyethylene Oxide WSR 303 and WSR N-60K, as well as HPMC K100M, showed moderately good flow characteristics with C.I. values ranging from 21.43% to 25% and AR values around 32–33°. Natural gums including Neem, Damar, and Copal exhibited relatively better flow with lower compressibility (C.I. 18.18–20%) and HR values close to 1.22, indicating favorable handling characteristics. Among the disintegrants, Cross Carmellose Sodium showed acceptable flow with a C.I. of 25%, whereas Crospovidone demonstrated poor flow with the highest C.I. (44.44%) and HR (1.8). Povidone K30 and talc showed moderate flow properties, while magnesium stearate displayed the poorest flow, reflected by the highest C.I. (46.67%) and HR (1.88), along with the steepest angle of repose (36° 20′). Overall, most excipients showed fair to good flow properties, whereas Crospovidone and magnesium stearate may require flow enhancers or granulation techniques during formulation.

The bilayer tablets provided rapid release of Gatifloxacin (90% within 45 minutes) and sustained release of Arbekacin up to 14 hours. Microspheres extended release to 24 hours, exhibiting an initial burst followed by diffusion-controlled release. Kinetic modeling confirmed Higuchi and Korsmeyer–Peppas models ($R^2 > 0.99$), indicating non-Fickian transport mechanisms governed by both diffusion and erosion. Entrapment efficiencies were high for both drugs (up to 89.4%), especially in formulation PM4, which also showed excellent buoyancy (94.6%). Antimicrobial testing demonstrated that optimized formulations retained drug activity and outperformed pure drugs in sustained inhibition zones. AGM7 showed the highest zone of inhibition (19 ± 0.9 mm), while AGM11 exhibited prolonged action despite a smaller initial zone (8 ± 1.03). This suggests effective synergy and extended therapeutic action against MDR pathogens. The relatively higher and sustained

inhibition zones observed in AGM7 and AGM4 suggested synergistic activity between Arbekacin and Gatifloxacin, especially when formulated using optimized polymer blends. The presence of extended inhibition zones, particularly for Gram-negative pathogens, validated the efficacy of the gastroretentive delivery systems in ensuring prolonged drug release and therapeutic action.

K. Bangsa Ihsan et al. developed floating microspheres of Ciprofloxacin, which showed buoyancy up to 8 hours and drug release for 12 hours (Arumugam et al., 2021). In contrast, our optimized formulations achieved >12 hours of floatation and 24-hour release, indicating a superior design for sustained therapy. Ramesh Pareek et al. reported Gatifloxacin release from matrix tablets with ~85% release in 12 hour (Pareek et al., 2019). Our study achieved ~90% in 45 minutes, while also combining it with sustained Arbekacin, offering a dual-phase therapeutic advantage. Our PEO-HPMC-based system improved entrapment up to 82.12%, with enhanced buoyancy and broad-spectrum antibacterial performance. Compared to previous studies, this system offered improved buoyancy, extended-release duration, and better antimicrobial activity, highlighting its promise for sustained UTI treatment with reduced dosing frequency and resistance risk.

The stability study of the formulation conducted over 90 days demonstrated consistent physical and chemical properties under accelerated storage conditions. Throughout the study period, no changes in appearance were observed, indicating excellent physical stability. The assay values for both Gatifloxacin and Arbekacin remained within the acceptable range of 95–105% of the label claim, showing only a slight and gradual decline—Gatifloxacin decreased from 97.8% to 96.9%, and Arbekacin from 98.3% to 97.3%, suggesting good chemical stability. Floating lag time remained within acceptable limits (≤ 2 minutes), with minimal variation (56 to 59 seconds), while total floating time consistently exceeded 12 hours, confirming the buoyancy stability of the formulation. Drug release profiles also remained stable, with Gatifloxacin releasing approximately 88–90% within 45 minutes and Arbekacin maintaining a sustained release of around 88–90% over 12 hours. The similarity factor (f2) values across 30, 60, and 90 days were above 50 (ranging from 72.1 to 65.7), indicating that the dissolution profiles remained similar over time. Overall, the formulation was found to be stable for at least 90 days under the tested conditions.

5. CONCLUSION

The present study successfully developed and evaluated gastroretentive bilayer tablets and floating microspheres co-loaded with Arbekacin and Gatifloxacin for targeted treatment of UTIs. The bilayer tablet system enabled rapid initial release of Gatifloxacin to achieve effective plasma concentrations, while the floating microspheres sustained the release of Arbekacin over 24 hours, ensuring prolonged therapeutic action. The optimized formulations exhibited high entrapment efficiency, excellent in vitro buoyancy (>12 h), and favorable release kinetics characterized by non-Fickian diffusion. Stability studies confirmed the formulations-maintained drug content, floating behavior, and release profiles over 90 days. Antibacterial studies revealed enhanced efficacy and synergistic inhibition against uropathogens. This drug delivery system demonstrates strong potential for improving therapeutic outcomes and patient adherence in the management of resistant UTIs—a growing global health concern amid rising antimicrobial resistance. However, the study is limited to in vitro and preliminary stability evaluations. Further in vivo pharmacokinetic and clinical studies are warranted to confirm the translational applicability of the formulation. Nonetheless, this work provides a promising foundation for the development of combination gastroretentive systems aimed at tackling antimicrobial resistance in clinical settings.

CONFLICT OF INTEREST

All authors declared no conflict of interest.

FUNDING SOURCES

No fund was received for this research.

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