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ZETA-SIZE DEPENDENT AND *IN-VITRO* DISSOLUTION PERFORMANCE OF AMOXICILLIN AND METRONIDAZOLE LOADED FRUIT-BASED NANOPARTICLES

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ABSTRACT

Background: The therapeutic performance of antimicrobial agents such as metronidazole and amoxicillin is often limited by suboptimal dissolution and bioavailability. Green nanotechnology offers a sustainable strategy to enhance drug delivery through size-controlled nanoparticle systems.

Objective: This study evaluated the zeta–size dependent performance and *in-vitro* dissolution behaviour of metronidazole and amoxicillin loaded fruit-based nanoparticles synthesized using *Carica papaya* and *Musa acuminata* extracts.

Methods: Nanoparticles were prepared via green synthesis using silver nitrate as a precursor. Particle size was determined using a Zetasizer, while in-vitro dissolution studies were conducted using a USP rotating paddle apparatus in 0.1N HCl at 37 ± 1°C. Drug quantification was performed spectrophotometrically, and results were compared with innovator (IB) and generic (GB) commercial brands. Statistical analysis was performed using SPSS version 20.

Results: The nanoparticles exhibited sizes within the nanometric range (33.93–69.42 nm for amoxicillin and 52.72–93.87 nm for metronidazole), confirming successful nanoformulation. Dissolution profiles demonstrated enhanced drug release in most test batches compared to commercial products. Amoxicillin batch PA2b achieved 90.3% release at 60 min versus 84% (IB) and 64% (GB). Metronidazole batch PM3b showed 94.3% release at 60 min, exceeding 86% (IB) and 69% (GB). Silver nitrate exhibited sustained release alongside antibiotic release, suggesting potential synergistic antimicrobial effects.

Conclusion: Fruit-mediated green synthesis produced stable nanosized formulations with significantly improved dissolution profiles, indicating potential enhancement in bioavailability and therapeutic efficacy.

KEYWORDS: Green nanotechnology, Metronidazole nanoparticles, Amoxicillin nanoparticles, Zeta-size performance, *In-vitro* dissolution.

1. INTRODUCTION

The performance of metronidazole-loaded fruit-based nanoparticles (NPs) is critically influenced by their physicochemical properties, particularly particle size and zeta potential (collectively referred to as zeta-size dependent performance). These parameters determine colloidal stability, drug encapsulation efficiency (EE), drug release kinetics, cellular uptake, antimicrobial activity, and biocompatibility. key factors that govern therapeutic efficacy in treating anaerobic bacterial and protozoal infections.[1,2] Zeta potential reflects surface charge and electrostatic repulsion between particles, while size affects surface area, dissolution rate, and biodistribution. Optimal zeta-size profiles are essential for preventing aggregation, prolonging circulation, and enhancing targeted delivery of metronidazole, which suffers from poor solubility, short half-life, and gastrointestinal side effects.[3]

Particle Size and Its Impact, smaller particle size (typically 20–200 nm) increases surface area-to-volume ratio, accelerating dissolution and improving bioavailability.[4] Bawazeer et al. (2022) synthesized black pepper fruit-derived gold nanoparticles (AuNPs) with sizes of 20–50 nm, exhibiting high stability (PDI 0.2–0.3) and catalytic/antimicrobial activity.[5] When loaded with metronidazole, smaller sizes enhanced cellular uptake and biofilm penetration, reducing MIC against *Porphyromonas gingivalis* by 50–75%.[3] Hossain et al. (2019) reported lemon fruit ZnONPs at 30 nm, with DLS confirming PDI of 0.25 and sustained release over 24 hours, improving dissolution of encapsulated antibiotics.[6] Larger particles (>200 nm) often show reduced EE and faster clearance, while ultra-small sizes (<10 nm) risk toxicity.[7]

Zeta potential and colloidal stability, Zeta potential values of ±25–35 mV indicate strong electrostatic repulsion, preventing aggregation and ensuring long-term stability.[8] Jahura et al. (2025) reported chitosan nanoparticles loaded with metronidazole and ciprofloxacin, achieving zeta potentials of −30 to −40 mV, resulting in EE >90% and prolonged release (48 hours, Higuchi model $R^2 = 0.95$).[9] Negative zeta from fruit capping (e.g., polyphenols) enhances stability in physiological pH, reducing opsonization and extending circulation time.[10] (Pathak & Akhtar, 2018). Cadinoiu et al. (2025) found metronidazole-loaded chitosan NPs with zeta −28 mV exhibited excellent stability and MIC reduction against *Clostridium perfringens* (from 8 to 4 μg/mL), attributed to electrostatic interactions with bacterial membranes.[11]

Optimal performance occurs when size and zeta potential synergize. Smaller particles with high absolute zeta (>±30 mV) show superior dissolution and antimicrobial activity due to increased surface exposure and repulsion.[4] Steckiewicz et al. (2022) reported silver NPs (30–80 nm, zeta −35 mV) loaded with metronidazole achieved synergistic biofilm inhibition (>80%) against periodontitis pathogens.[3] Larger particles with low zeta (<±20 mV) aggregate, reducing EE and release control.[12] Fruit-based NPs often achieve this balance, with lemon-derived ZnONPs (30 nm, −25 mV) showing sustained release and low cytotoxicity (<5% hemolysis at 100 μg/mL).[6]

Hence, zeta-size dependent performance is pivotal for metronidazole-loaded fruit-based NPs, driving stability, dissolution, and antimicrobial efficacy. Performance evaluation encompasses physicochemical characterization, in vitro release, antimicrobial activity, and biocompatibility.[6] This research highlights their potential as sustainable alternatives, paving the way for advanced formulations in Nigeria.

2. METHODS

2.1 Particle Size Analysis (Zeta-sizer measurements of Nanoparticles)

Nanodrug zeter-size analysis was carried out to determine the particle size of the nanodrugs samples using Zeter Sizer instrument. About 1 mg/ml of each nanodrug sample was obtained. Zeta Sizer cell was selected and the cell was filled with 1mg/ml nanodrug sample and an SOP measurement of the nanodrug sample was made and the cell was inserted into the instrument and the temperature was allowed to stabilize after which the nanoparticle size was measured and results displayed and saved to the measurement file.

2.2 Release Studies of Drug-Loaded Fruit-Based Nanoparticles

2.2.1 Standard Calibration Curve for Amoxicillin, Metronidazole and Silver nitrate ($AgNO_3$)

To make a stock solution; a 100 mg quantity of each of the pure drug samples was dissolved and made up to 100 mL in a 100 mL volumetric flask using 0.1N HCl. Serial dilution of the stock solution was made to obtain diluted solutions. Subsequently, scan of the solutions was carried out using an UV/Vis Spectrophotometer (JenWay Model 6405), the wavelengths of maximum absorption were obtained as; 240 nm, 243 nm and 217 nm for amoxicillin, metronidazole and silver nitrate respectively. The absorbance of the serially diluted pure drug samples solutions was obtained at 240 nm, 243 nm and 217 nm respectively. The absorbance readings of the different concentration were used to plot the Beer-Lamberts calibration curve.

2.2.2 *In-Vitro* Dissolution Profile of the Formulated Drug-Loaded Fruit-Based Nanoparticles (Test Samples) and the Commercially available Drugs as Standard Drug Samples (Generic and Innovative Brands of Amoxicillin and Metronidazole; GB, IB)

1. The dissolution profile for each batch of amoxicillin and metronidazole nanocapsules, generic and innovative brands of amoxicillin and metronidazole was carried out using a six-station rotating paddle dissolution apparatus [Erweka® DT600 High Head (DT600HH), Germany], the rotating paddle method was adopted. The dissolution medium constituted 900 mL of 0.1N HCl solution maintained at 37 ± 1 ^{o}C with paddle speed maintained at 50 rpm. A 5 mL sample solution was withdrawn at predetermined intervals of 2, 5, 10, 15, 20, 25, 30, 40, 50, 60 minutes respectively. The withdrawn sample solution was replaced with the same volume of 0.1N HCl at each sampling time and maintained at the same temperature. The absorbance of each sampled solution was read in a UV spectrophotometer (Jenway Spec, Model 6405, England) at wavelengths of 240 nm, 243 nm and 217 nm respectively.

2.3 Statistical Software

Statistical software called statistical package for the social science (SPSS) version 20 was used statistically to analyze the generated dissolution data.

3. RESULTS AND DISCUSSION

3.1 Nanoparticles Size (nm) of Amoxicillin and Metronidazole Loaded Fruit-Based Nanoparticles

3.1.1 Nanoparticle Size (nm) of Amoxicillin Loaded C*arica papaya* and *Musa acuminata*-Based Nanoparticles

Figure 3.1 illustrates the nanoparticle size (nm) of amoxicillin loaded *carica papaya* and *musa acuminate*-based nanoparticles.

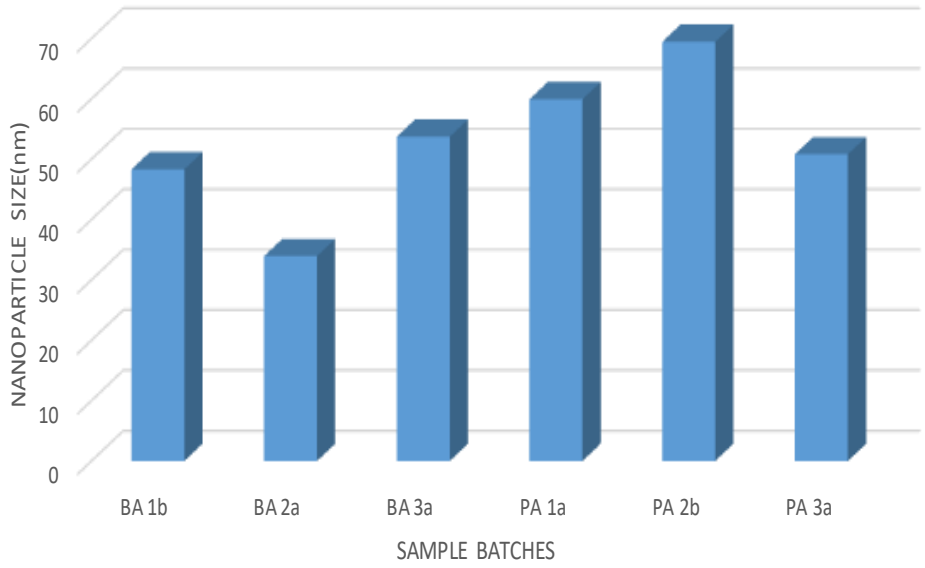

Figure 3.1: Nanoparticle size (nm) of amoxicillin loaded *carica papaya* and *musa acuminate*-based nanoparticles.

Nano-sizes for sample batches BA1b–PA3a are 48.29, 33.93, 53.70, 59.91, 69.42 and 50.79 nm respectively. These zeta sizes are within the specified size for nanoparticles and nanomaterial, which is 10–100 nm and 10–150 nm, respectively (Dahman *et al*., 2017).

3.1.2 Nanoparticle Size (nm) of Metronidazole-Loaded C*arica papaya* and *Musa acuminata*-Based Nanoparticles

Figure 3.2 illustrates the nanoparticle size (nm) of metronidazole-loaded *carica papaya* and *musa acuminate*-based nanoparticles.

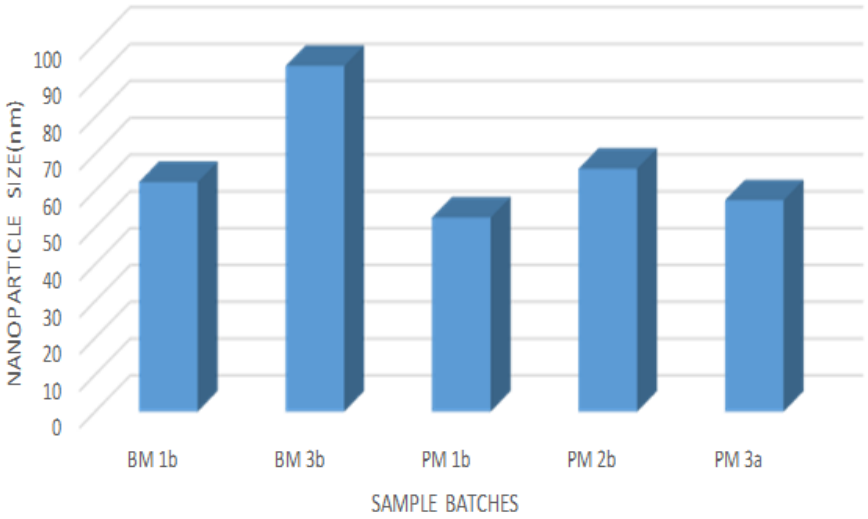

Figure 3.2: Nanoparticle size (nm) of metronidazole-loaded *musa acuminate and carica papaya* - based nanoparticles.

Nano-sizes for sample batches BM1b – PM3a are 62.36, 93.87, 52.72, 65.97 and 57.39 nm respectively. These zeta sizes are within the specified size for nanoparticles and nanomaterials, which is 10 – 100 nm and 10 – 150 nm, respectively (Dahman *et al*., 2017).

Nanoparticle size highly depends on the pH values of the fruit-based generated nanoparticles including processing factors such as temperature, stirring rate, therefore effect on the size of nanoparticles could be due to the variation in the process variables. Hence, the average diameter of synthesized silver nanoparticles obtained ranged between 33.9–69.4 nm for Amoxicillin nanomedicine and nanoparticle size range of 52.7–93.9 nm for the Metronidazole nanomedicine. Stirring time affects nanoparticle size and causes significant decrease when the stirring speed increases and also as the temperature decreases. Hence, a direct correlation exists between particle size and temperature of preparation. However, nanoparticles aggregated after freeze drying process and excellently exhibited good physical stability in the solid state (Honary *et al.*, 2011).

3.1.3 *In-Vitro* Dissolution Profile of Respective Synthesized Amoxicillin and Metronidazole-Loaded Fruit-Based Nanoparticles (Test Samples) and Commercially Available Drugs as Standard Samples; Innovator Brand and Generic Brand (IB and GB)

3.1.3.1 *In-Vitro* Drug Release of Amoxicillin, Metronidazole and Silver nitrate respectively from Test Samples

Figures 4.49-54 illustrate the in-vitro drug release of amoxicillin, metronidazole and silver nitrate respectively from test samples.

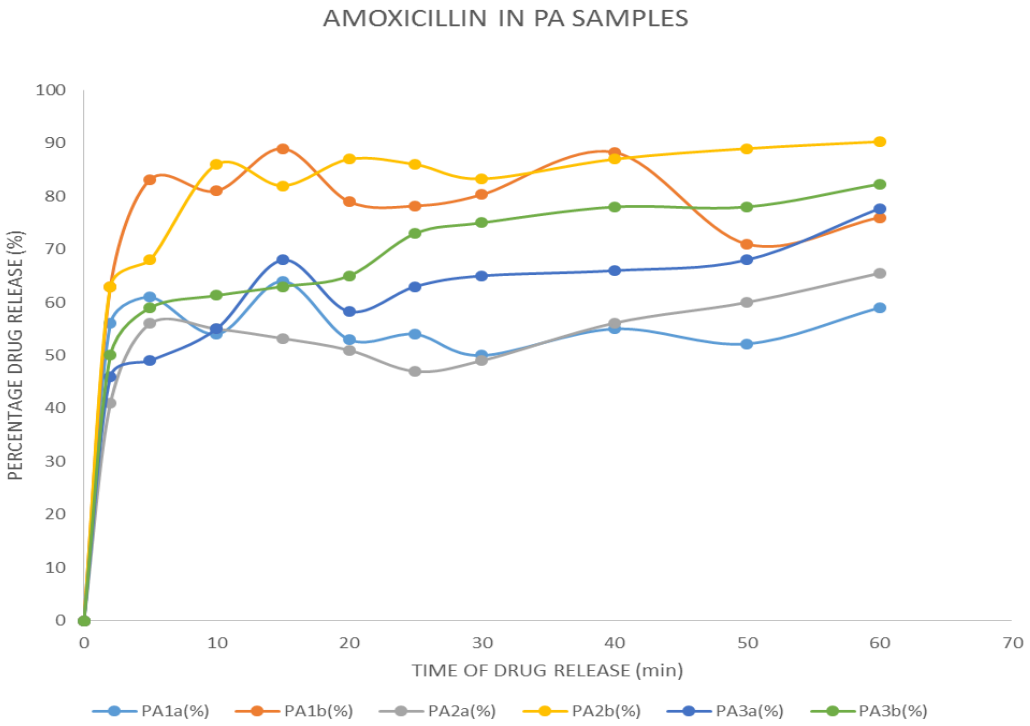

Figure 3.3: Amoxicillin release profile of the amoxicillin-loaded *Carica papaya*–based nanoparticles.

Key: PA; P – Pawpaw (*Carica papaya*), A - Amoxicillin, 1, 2, 3 – 1st, 2nd, 3rd dose of amoxicillin pure sample (75 mg, 125 mg, 250 mg), a, b – 2.5 % w/v, 5.0 % w/v of $AgNO_3$ (1st, 2nd, 3rd concentration of silver nitrate respectively).

For sample batch PA1a, 64 % of amoxicillin was released into the dissolution medium at 15 min and was the peak drug released. For sample batch PA1b, 89 % of amoxicillin was released into the dissolution medium at 15 min and was the peak drug released. Sample batch PA2b had it peak release at 60 min, 90.3 %.

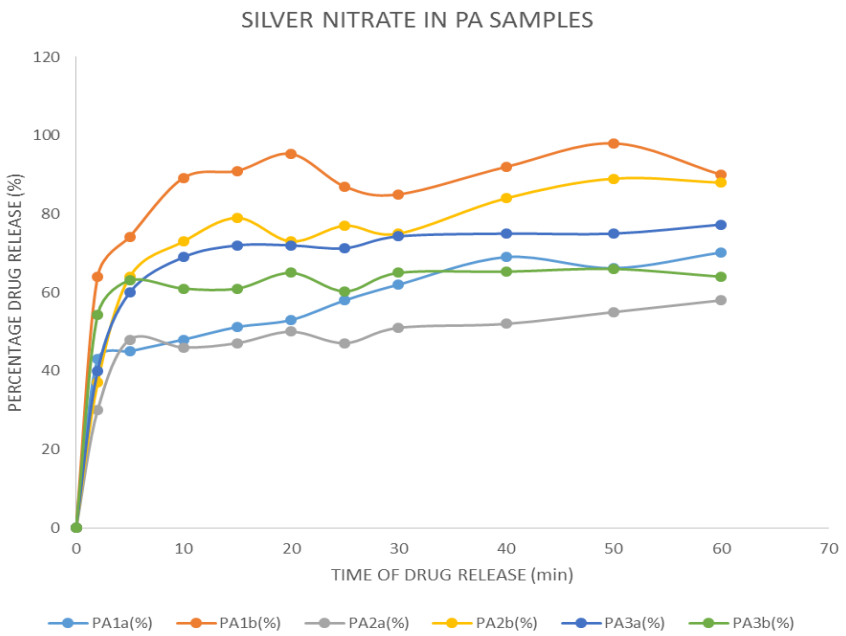

Figure 3.4: Silver nitrate release profile of the amoxicillin-loaded *Carica papaya*–based nanoparticles.

Key: PA; P – Pawpaw (*Carica papaya*), A - Amoxicillin, 1, 2, 3 – 1st, 2nd, 3rd dose of amoxicillin pure sample (75 mg, 125 mg, 250 mg), a, b – 2.5% w/v, 5.0% w/v of $AgNO_3$ (1st, 2nd, 3rd concentration of silver nitrate respectively).

For sample batch PA1b, 91 % of silver nitrate was released at 15 min and 90 % released at 60 min. Sample batch PA2b released 89 % of silver nitrate at 50 min and that was the peak release for this batch. For sample batch PA3b, at 60 min, 77.3 % of silver nitrate was released into the dissolution medium and was the peak release for this batch.

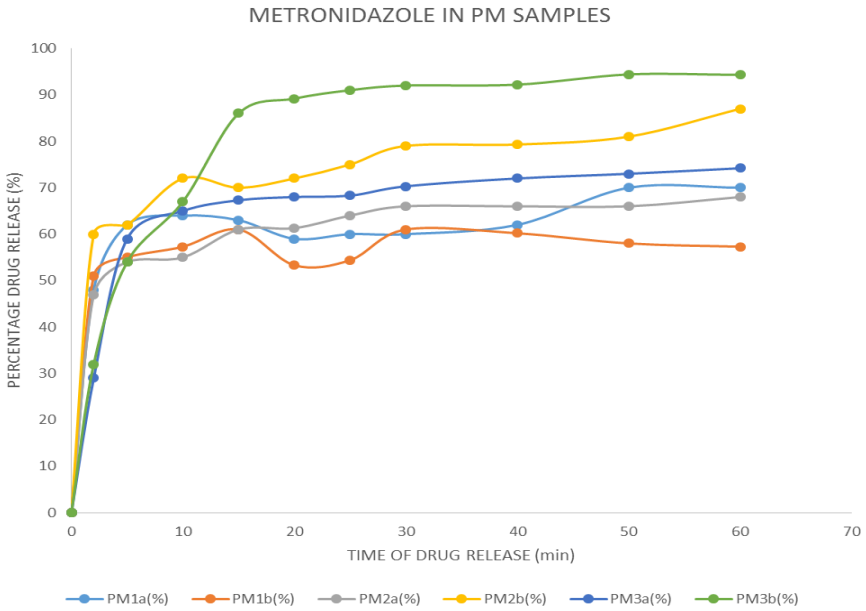

Figure 3.5: Metronidazole release profile of the metronidazole-loaded *Carica papaya*–based nanoparticles.

Key: PM; P – Pawpaw (*Carica papaya*), M - Metronidazole, 1, 2, 3 – 1st, 2nd, 3rd dose of metronidazole pure sample (50 mg, 100 mg, 200 mg), a, b – 2.5 % w/v, 5.0 % w/v of $AgNO_3$ (1st, 2nd, 3rd concentration of silver nitrate respectively).

For sample batch PM1a, 70 % of metronidazole was first released into the dissolution medium at 50 min and was the peak release for the batch. For sample batch PM2a, 68 % of metronidazole was released into the dissolution medium at 68 min. For batch PM2b, 87 % of metronidazole was released at 60 min. The peak release was 92.2 % at 40 min for batch PM3b.

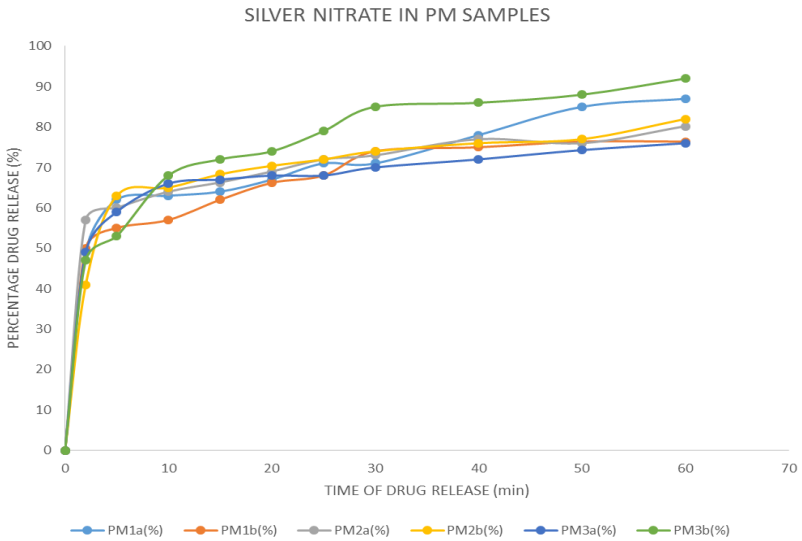

Figure 3.6: Silver nitrate release profile of the metronidazole-loaded *Carica papaya*–based nanoparticles

Key: PM; P – Pawpaw (*Carica papaya*), M - Metronidazole, 1, 2, 3 – 1st, 2nd, 3rd dose of Metronidazole pure sample (50 mg, 100 mg, 200 mg), a, b – 2.5 % w/v, 5.0 % w/v of $AgNO_3$ (1st, 2nd, 3rd, concentration of silver nitrate respectively).

For sample batch PM1a, 87 % of silver nitrate was released into the dissolution medium at 60 min and was the peak release. For sample batch PM1b, 76.4 % of silver nitrate was released into the dissolution medium at 50 min. For sample batches PM2a, PM2b, PM3a, PM3b, 80.2 %, 82 %, 76 % and 92 % of silver nitrate was respectively released at 60 min.

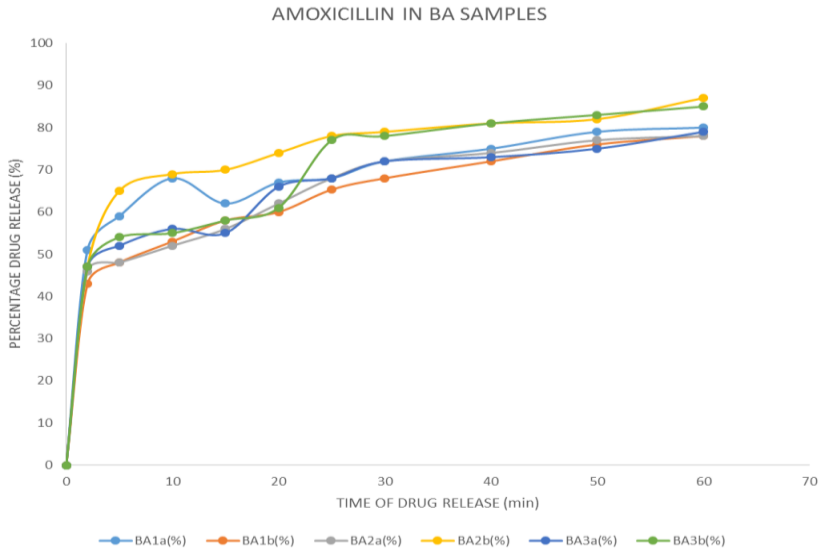

Figure 3.7: Amoxicillin release profile of the amoxicillin loaded *Musa acuminata*–based nanoparticles.

Key: BA; B – Banana (*Musa acuminata*), A - Amoxicillin, 1, 2, 3 – 1st, 2nd, 3rd dose of amoxicillin pure sample (75 mg, 125 mg, 250 mg), a, b – 2.5 % w/v, 5.0 % w/v of $AgNO_3$ (1st, 2nd, 3rd, concentration of silver nitrate respectively).

For sample batch BA1a, 80 % of amoxicillin was released into the dissolution medium at 60 min and was the peak release for this batch. For sample batch BA1b, 78 % of amoxicillin was released into the dissolution medium at 60 min. For sample batch BA2a, BA3a and BA3b, 78 %, 79 %, 85 % of amoxicillin was respectively released at 60 min and the peak drug release was observed in batch BA3b.

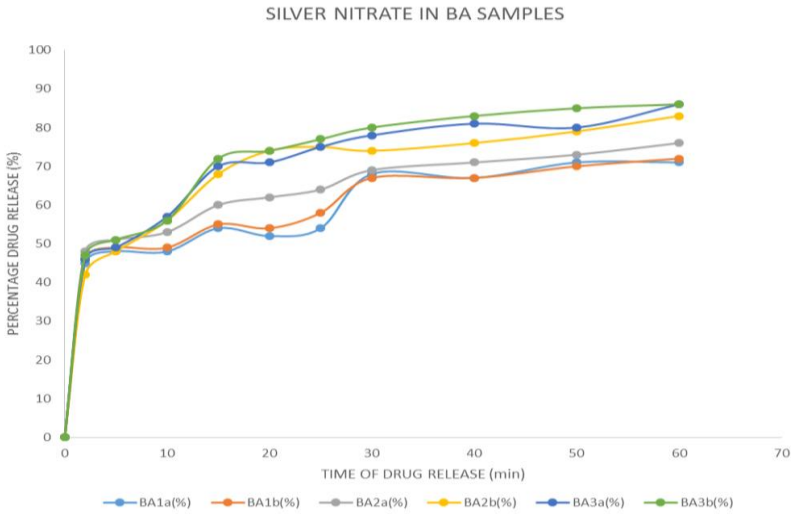

Figure 3.8: Silver nitrate release profile of the amoxicillin-loaded *Musa acuminata*–based nanoparticles.

Key: BA; B – Banana (*Musa acuminata*), A - Amoxicillin, 1, 2, 3 – 1st, 2nd, 3rd dose of amoxicillin pure sample (75 mg, 125 mg, 250 mg), a, b – 2.5 % w/v, 5.0 % w/v of $AgNO_3$ (1st, 2nd, 3rd, concentration of silver nitrate respectively).

For sample batch BA1a, 71 % of silver nitrate was released into the dissolution medium at 50 min. For sample batch BA1b, 72 % of silver nitrate was released into the dissolution medium at 60 min. For sample batch BA2a, BA2b, BA3a and BA3b, 75.8 %, 83 %, 86 % and 86 % of silver nitrate was respectively released at 60 min, and the peak release of silver nitrate occurred at 60 min for sample batches BA3a and BA3b respectively.

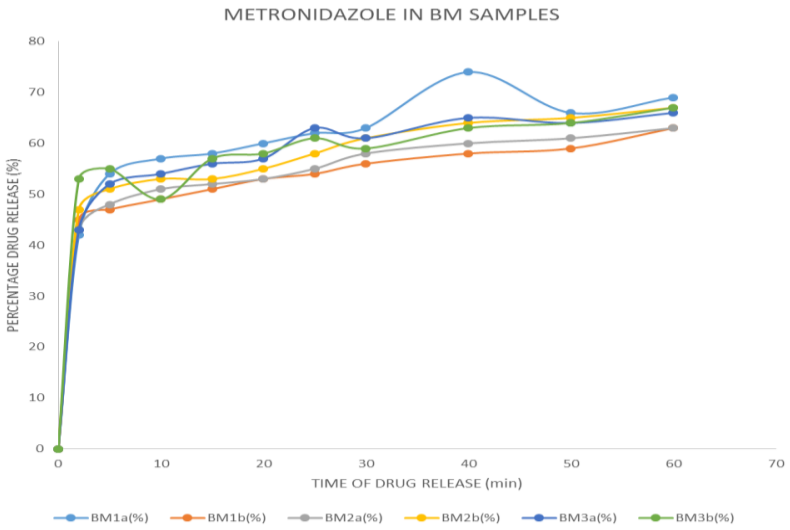

Figure 3.9: Metronidazole release profile of metronidazole-loaded *Musa acuminata*–based nanoparticles.

Key: BM; B – Banana (*Musa acuminata*), M - Metronidazole, 1, 2, 3 – 1st, 2nd, 3rd dose of Metronidazole pure sample (50 mg, 100 mg, 200 mg), a, b – 2.5 % w/v, 5.0 % w/v of $AgNO_3$ (1st, 2nd, 3rd, concentration of silver nitrate respectively).

For sample batches BM1a, BM1b, BM2a, BM2b, BM3a and BM3b, 69 %, 63 %, 62.8 %, 67 %, 66 % and 67 % of metronidazole was respectively released into the dissolution medium at 60 minutes and the peak metronidazole release was observed at 69 % for batch BM1a.

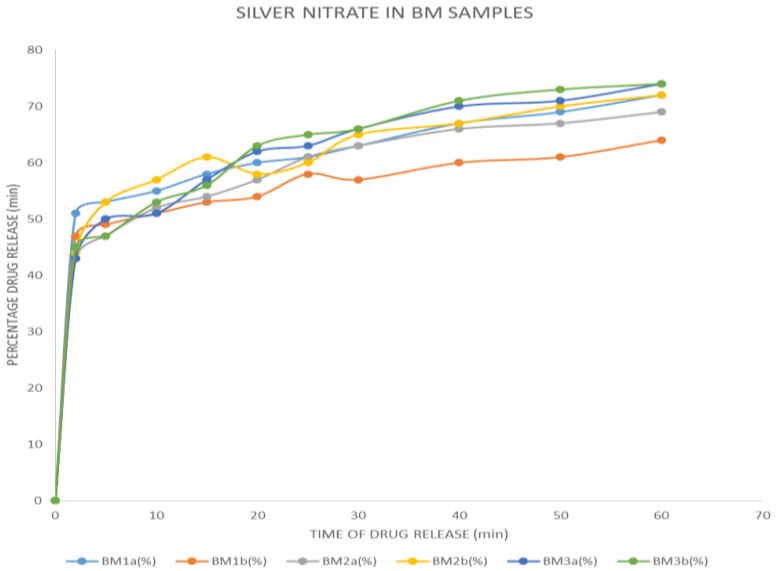

Figure 3.10: Silver nitrate release profile of metronidazole-loaded *Musa acuminata*–based nanoparticles.

Key: BM; B – Banana (*Musa acuminata*), M - Metronidazole, 1, 2, 3 – 1st, 2nd, 3rd dose of Metronidazole pure sample (50 mg, 100 mg, 200 mg), a, b – 2.5 % w/v, 5.0 % w/v of $AgNO_3$ (1st, 2nd, 3rd, concentration of silver nitrate respectively).

For sample batch BM1a, BM1b, BM2a, BM2b, BM3a and BM3b, showed metronidazole drug release at 72 %, 64 %, 69 %, 72 %, 74 % and 73.5 % respectively. The peak drug release was observed at 74 % for batch BM3a.

3.1.3.2 *In-Vitro* Drug Release of Amoxicillin and Metronidazole respectively from Commercially Available Drugs as Standard Drugs and Test Samples

Figures 3.11-3.14 illustrate the in-vitro drug release of amoxicillin and metronidazole, respectively from commercially available drugs as standard drugs and test samples.

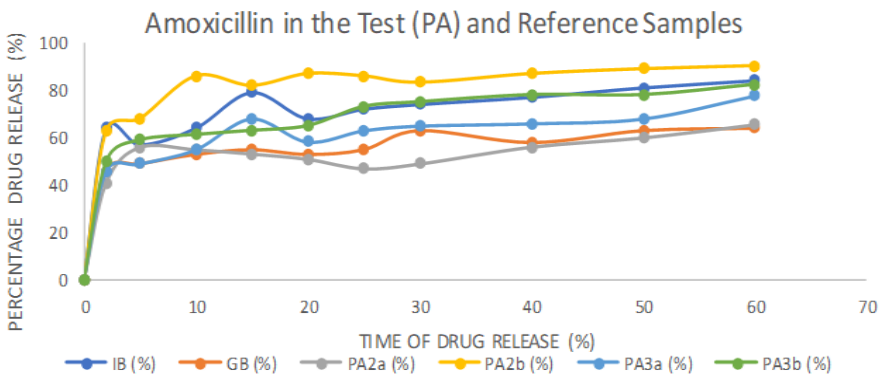

Figure 3.11: Amoxicillin release profile of commercially available drugs as standard drugs and PA test samples respectively.

Key: IB-Innovator brand, GB-Generic brand (IB, GB: commercially available drugs as standard drugs), PA; P – Pawpaw (*Carica papaya*), A - Amoxicillin, 2, 3 – 2nd, 3rd dose of amoxicillin pure sample (125 mg, 250 mg), a, b – 2.5 % w/v, 5.0 % w/v of $AgNO_3$ (1st and 2nd, concentration of silver nitrate respectively).
PA2a, PA2b, PA3a and PA3b (test samples).

For commercially available drugs as standard drug batches IB and GB; for IB, 84 % of amoxicillin was released into the dissolution medium at 60 min and was the peak release for the IB batch and for GB, 64 % was released into the dissolution medium at 60 min. For test sample batches; PA2a, 65.5 % of amoxicillin was released into the dissolution medium at 60 min, PA2b batch released 90.2 % of amoxicillin at 60 min, PA3a batch released 77.7 % of amoxicillin at 60 min and PA3b batch released 82.3 % of amoxicillin at 60 min. However, the test sample batch PA2b showed the peak amoxicillin release of 90.3 and PA3b also showed a good amoxicillin release at 82.3 % relatively close to the percentage release of the reference sample which showed amoxicillin release of 84 % all at 60 min. Hence, the amoxicillin-loaded fruit-based nanoparticles is evaluated to have higher efficacy compared to the reference samples and this difference is as a result of the formulation technique (science) used in the formulation of nanoparticles (test samples). The technique is nanotechnology and green-synthesis method.

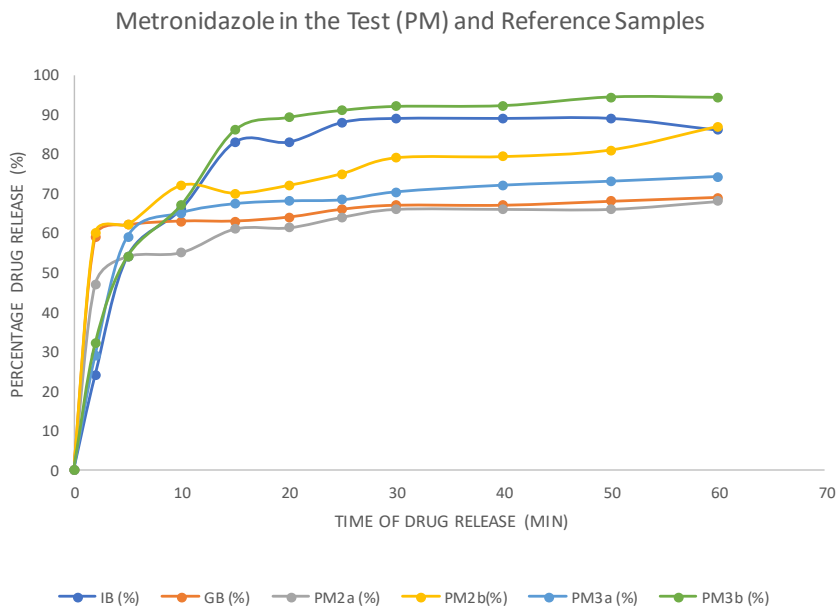

Figure 3.12: Metronidazole release profile of commercially available drugs as standard drugs and PM test samples respectively

Key: IB-Innovator brand, GB-Generic brand (commercially available drugs as standard drugs), PM; P – Pawpaw (*Carica papaya*), M - Metronidazole, 2, 3 – 2nd and 3rd dose of amoxicillin pure sample (100 mg, 200 mg), a, b – 2.5 % w/v, 5.0 % w/v of $AgNO_3$ (1st and 2nd, concentration of silver nitrate respectively).
PM2a, PM2b, PM3a and PM3b (test samples).

For commercially available drugs as standard drugs batches IB and GB; for IB, 88 %, 89 % and 86 % of metronidazole was released into the dissolution medium at 25, 30 and 60 min respectively, and 89 % was the peak release for the IB batch at 30 min. For GB, 69 % was released into the dissolution medium at 60 min. For test sample batches; PM2a, 68

% of metronidazole was released into the dissolution medium at 60min, PM2b batch released 87 % of metronidazole at 60 min, PM3a batch released 74.2 % of metronidazole at 60 min and PM3b batch released 94.3 % of metronidazole at 60 min.

However, the test sample batch PM3b showed the peak metronidazole release of 94.3 and PA2b also showed a good metronidazole release at 87 % relatively higher than the percentage release of the commercially available drugs as standard drugs (IB; innovator brand) which showed metronidazole release of 86 % all at 60 min.

Hence, the metronidazole-loaded fruit-based nanoparticles was evaluated to have higher dissolution rate which points that the test samples possibly might have higher bioavailability and efficacy compared to the commercially available drugs as standard drugs and this difference is as a result of the formulation technique (science) used in the preparation of nanoparticles (test samples). Nanotechnology technique and green-synthesis method were used during the nanoparticles formulation processes.

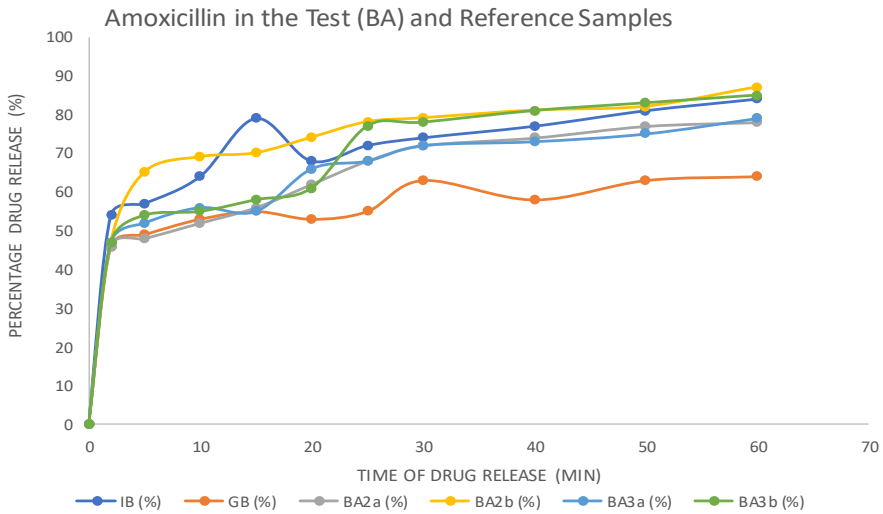

Figure 3.13: Amoxicillin release profile of commercially available drugs as standard drugs and BA test samples respectively.

Key: IB-Innovator brand, GB-Generic brand (IB, GB: commercially available drugs as standard drugs), BM; B – Banana (*Musa acuminata*), A - Amoxicillin, 2, 3 – 2nd and 3rd dose of amoxicillin pure sample (100 mg, 200 mg), a, b – 2.5 % w/v, 5.0 % w/v of $AgNO_3$ (1st and 2nd, concentration of silver nitrate respectively).
BA2a, BA2b, BA3a and BA3b (test samples).

For commercially available drugs as standard drugs IB and GB; for IB, 84 % of amoxicillin was released into the dissolution medium at 60 min, and was the peak release for the commercially available drugs as standard drugs. For GB, 64 % was released into the dissolution medium at 60 min. For test sample batches; BA2a, 78 % of amoxicillin was released into the dissolution medium at 60min, BA2b batch released 87 % of amoxicillin at 60 min, BA3a batch released 79 % of amoxicillin at 60 min and BA3b batch released 85 % of metronidazole at 60 min. However, the test sample batch BA2b showed the peak amoxicillin release of 87 % and BA3b showed a good amoxicillin release at 85 % relatively close to the percentage release of the commercially available drugs as standard drugs (IB) which showed amoxicillin release of 84 % at 60 min. Hence, the amoxicillin-loaded fruit-based nanoparticles (test samples) was

evaluated to have higher dissolution rate which points that the test samples possibly might have higher bioavailability and efficacy compared to the commercially available drugs as standard drugs and this difference is as a result of the formulation technique (science) used in the formulation of nanoparticles (test samples). Nanotechnology technique and green-synthesis method were used during the nanoparticles formulation processes.

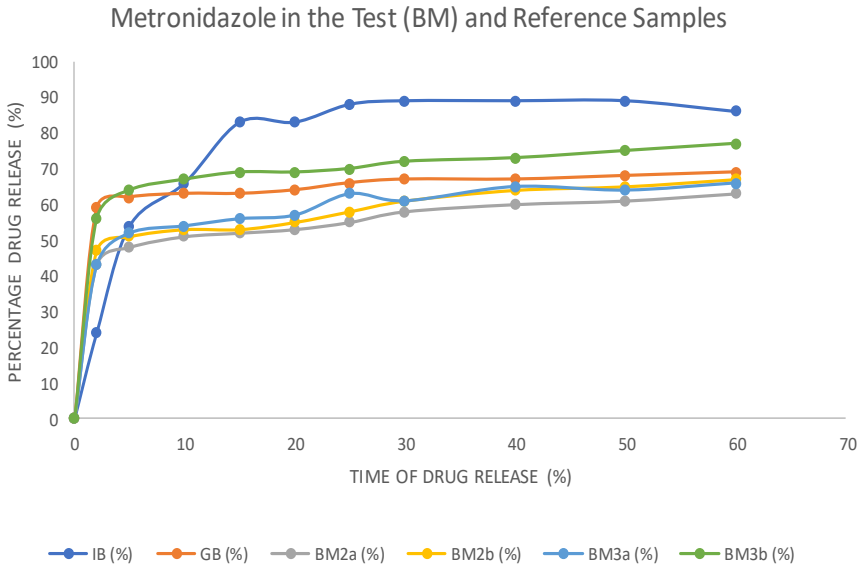

Figure 3.14: Metronidazole release profile of and commercially available drugs as standard drugs BM test samples respectively.

Key: IB-Innovator brand, GB-Generic brand (IB, GB: commercially available drugs as standard drugs), BM; B – Banana (*Musa acuminata*), M - Metronidazole, 2, 3 – 2nd and 3rd dose of metronidazole pure sample (100 mg, 200 mg), a, b – 2.5 % w/v, 5.0 % w/v of $AgNO_3$ (1st and 2nd, concentration of silver nitrate respectively).
BM2a, BM2b, BM3a and BM3b (test samples).

For commercially available drugs as standard drugs batches IB and GB; for IB, 88 %, 89 % and 86 % of metronidazole was released into the dissolution medium at 25, 30 and 60 min respectively, and 89 % was the peak release for the IB batch at 30 min. For GB, 69 % was released into the dissolution medium at 60 min. For test sample batches; BM2a, 63 % of metronidazole was released into the dissolution medium at 60min, BM2b batch released 67 % of metronidazole at 60 min, BM3a batch released 66 % of metronidazole at 60 min and BM3b batch released 77 % of metronidazole at 60 min. However, the test sample batch BM3b showed the peak metronidazole release amongst all the test sample batches. Generally, majority of the test samples showed better and improved dissolution rate compared to the commercially available drugs as standard drugs and this is an impressive outcome and an inference that test samples possibly would have greater and improved bioavailability and efficacy as against the commercially available drugs as standard drugs and these improved attributes are traceable to the formulation technique (science) used in the formulation of nanoparticles (test samples). Nanotechnology technique and green-synthesis method were used during the nanoparticles formulation processes.

4. CONCLUSION

This study systematically evaluated the zeta–size dependent performance and *in-vitro* dissolution behaviour of amoxicillin and metronidazole loaded fruit-based nanoparticles synthesized using green nanotechnology approaches.

The findings (results) clearly demonstrate that the physicochemical characteristics and release performance of the formulated nanoparticles are strongly influenced by particle size distribution and formulation variables. Particle size analysis confirmed that all synthesized batches of amoxicillin and metronidazole loaded nanoparticles prepared using *Carica papaya* and *Musa acuminata* extracts fell within the nanometric range (33.93–69.42 nm for amoxicillin formulations and 52.72–93.87 nm for metronidazole formulations). These sizes are within the internationally accepted nanoparticle range (10–100 nm), indicating successful nano-formulation. The observed size variations were attributable to differences in formulation parameters such as pH, temperature, stirring rate, and silver nitrate concentration. Importantly, the nanoscale dimensions achieved are expected to enhance surface area-to-volume ratio, dissolution rate, and ultimately drug bioavailability. Despite aggregation tendencies after freeze-drying, the nanoparticles exhibited acceptable solid-state stability.

In-vitro dissolution studies revealed significant enhancement in drug release from most nanoparticle formulations compared to commercially available innovator (IB) and generic (GB) brands. For amoxicillin-loaded *Carica papaya* nanoparticles, batch PA2b achieved a peak release of 90.3% at 60 minutes, exceeding the innovator brand (84%) and generic brand (64%). Similarly, *Musa acuminata*-based formulations (BA2b and BA3b) demonstrated release profiles (87% and 85% respectively) comparable to or superior to the innovator product. Metronidazole-loaded nanoparticles exhibited even more pronounced improvements. Batch PM3b showed a peak release of 94.3% at 60 minutes, surpassing both the innovator brand (86% at 60 min) and the generic product (69%). Although *Musa acuminata*-based metronidazole formulations demonstrated moderate release (maximum 77% in BM3b), they still compared favourably with the generic brand and demonstrated sustained release behaviour. The enhanced dissolution profiles observed across most nanoparticle batches indicate improved drug dispersion and solubilization resulting from nanoscale size reduction and green synthesis-mediated stabilization. The incorporation of silver nitrate also contributed to controlled and sustained release characteristics, with consistent silver ion release profiles observed alongside antibiotic release, suggesting potential synergistic antimicrobial performance. Comparative evaluation with commercially available products confirms that the green-synthesized fruit-based nanoparticles generally demonstrated superior or comparable dissolution efficiency. This improvement is attributable to nanotechnology-driven particle size reduction, enhanced surface reactivity, and optimized drug matrix interaction. Given that dissolution rate is a critical determinant of oral bioavailability for poorly soluble drugs, these findings strongly suggest that the formulated nanoparticles may offer enhanced therapeutic efficacy.

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