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NATURAL RUBBER LATEX–BIOACTIVE GLASS COMPOSITE AS A DRUG DELIVERY SYSTEM FOR AMPICILLIN

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Abstract

This study evaluates Natural Rubber Latex (NRL)–Bioactive Glass (BG) Composites as carrier for ampicillin. Current drug delivery systems face challenges of uncontrolled release, poor biocompatibility, and unstable therapeutic levels. Incorporating bioactive glass into natural rubber latex was explored to improve compatibility, sustained release, and strength. Biomembranes (NRL with drug and NRL - BG with drug respectively) were polymerized at room temperature for 72 hours. The biomembranes were then characterized using fourier transmission – infrared (FT-IR) spectroscopy, scanning electron microscopy (SEM) and x-ray diffraction (XRD). The drug release mechanism through the skin, tensile strength and elongation at break were also evaluated. Results showed that 86.26% of the protein in the NRL was removed after centrifugation and the FTIR spectra analysis reveals no chemical interaction between the NRL, drug and bioglass as their individual characteristics exhibits solid fusion. Drug release reached about 70% with burst release near 52–54 hours. The mechanical analysis showed that the incorporation of the bioglass improved the tensile strength of the biomembrane significantly. The results confirm that natural rubber latex can act as a transdermal carrier for ampicillin, with bioactive glass further improving the delivery efficiency.

Keywords: natural rubber latex, bioactive glass, ampicillin

1. Introduction

A drug delivery system is a core aspect of pharmaceutical science concerned with the transport and controlled release of therapeutic agents to achieve a desired pharmacological effect while minimizing adverse effects and optimizing pharmacokinetics and biodistribution [1,2]. Different types of delivery platforms include oral systems, parenteral systems, transdermal systems, inhalation systems, targeted carrier-based systems, and controlled-release matrices. The principal goals of a drug delivery system are to control the release rate, improve bioavailability, target the drug to the site of action, and reduce systemic toxicity [3]. Transdermal delivery in particular can provide sustained systemic exposure, avoid first-pass hepatic metabolism, and improve patient compliance for chronic therapies [4,5].

Transdermal delivery systems provide a controlled release of drugs through the skin, making them suitable for chronic conditions requiring long-term therapy [6]. This route avoids first-pass hepatic metabolism and ensures more stable plasma drug concentrations. The patch, which is the most common form, typically consists of a protective backing layer, a drug reservoir or matrix, an adhesive, and sometimes a removable liner. Drug release occurs by diffusion across the skin, influenced by factors such as molecular size, lipophilicity, hydration, and skin barrier properties [7]. Natural rubber has been investigated as both an adhesive and a reservoir material because its porous structure supports drug embedding while maintaining strong adhesion [8].

Natural Rubber Latex (NRL) is primarily cis-1,4-polyisoprene, a renewable polymer valued for elasticity and adhesive strength in biomedical membranes [9]. Its residual proteins can induce allergenicity. Bioactive Glass (BG), typically composed of SiO_2–CaO–Na_2O–P_2O_5, reacts with physiological fluids to form hydroxyapatite, enhancing tissue bonding [10]. Calcium phosphate nanostructures also function as biodegradable carriers for sustained release. There have been reports of both NRL and BG being used as carrier drug delivery system. NRL has been used as biomembrane for controlled release system and the results has proven to be effective in biomedical applications [11]. The use of mesoporous BG in combination with medicines could serve as a multifunctional delivery platform for better osteogenesis and antimicrobial activities [12].

Ampicillin, despite broad antibacterial activity, exhibits poor stability, prompting encapsulation in polymeric matrices to improve therapeutic performance [13]. Various drug delivery systems have been developed, including polymeric nanoparticles, liposomes, micelles, etc., and most of these systems are associated with low drug loading, poor drug release kinetics, and potential toxicity [14]. To address these limitations, there is growing interest in simple, biocompatible, and mechanically robust materials capable of achieving sustained drug release without complex synthesis or high production costs. This gap provides the basis for exploring natural polymers combined with bioactive inorganic fillers as hybrid drug-delivery matrices.

In this context, combining NRL with bioactive glass offers a synergistic approach where NRL provides flexibility, film-forming capability, and high drug-entrapment potential, while bioactive glass contributes porosity, ion-exchange activity, and structural reinforcement. The resulting composite is expected to exhibit enhanced mechanical properties and more controlled drug diffusion compared to NRL or bioglass used separately.

Although NRL has been studied as a matrix for drug delivery and bioactive glass has been used in tissue-engineering and release systems, there is limited literature on their combined use as a single hybrid material. More specifically, no reported studies have evaluated NRL–bioglass composites for ampicillin loading and release, representing a clear knowledge gap that this work seeks to address.

Integrating NRL with bioactive glass offers a composite system combining mechanical resilience with bioactivity for controlled antibiotic delivery. Therefore, this research contributes to the expanding landscape of biomaterials and their applications in medicine. The findings of this work provide new insight into how the structure, mechanical behavior, and surface morphology of NRL–bioglass composites influence antibiotic release, offering a low-cost and biocompatible platform that may support future applications in wound therapy and sustained transdermal delivery.

2. Materials and Method

2.1. Materials

Materials used include: Natural rubber latex (NRL) (from Rubber Research Institute of Nigeria Iyanomo, Edo State), Ampicillin ($C_{16}H_{19}N_3O_4S$) capsule (from Laborate Pharmaceuticals India limited), Distilled water, Deionized water, and Bioglass ($40SiO_2 – 30Na_2O – 25CaO – 5P_2O_5$) prepared at the Department of Chemical and Food Science, School of Natural and Applied science, Bells University of Technology, Ota Ogun state.

2.2. Methods

2.2.1. Deproteinization

Deproteinization of the NRL was done using the procedure described by Herculano [10]. The NRL was centrifuged at 6000 rpm for 120 min. The cream fraction after centrifugation was redispersed to make the desired 60% of dry rubber content latex and then washed twice by centrifugation to reduce the protein content on the solution.

2.2.2. Drug Solution

Each gelatin capsule containing 250 mg of ampicillin trihydrate comprised 10 mg of the ampicillin drug powder diluted in 1 ml of distilled water to produce a solution of 10 mg/ml available in gelatin capsules without excipients.

2.2.3. Preparation of Biomembrane

Four different Biomembrane samples were prepared:

Table 1. Composition of Biomembrane.

Biomembrane	Composition
1	6ml Deproteined NR
2	6ml Deproteinized NR + 1g BG
3	6ml Deproteinized NR + 4 ml (10 mg/ml) ampicillin
4	6ml Deproteinized NR + 1g BG + 4 ml (10 mg/ml) ampicillin

The mixture was homogenized, poured into a petri dish and was left at room temperature for 72 hours to polymerize.

2.2.4. Characterization

The biomembranes were characterized using standard analytical techniques. Tensile strength and elongation at break were measured with a Universal Testing Machine according to ASTM protocols. Functional groups were identified by Fourier Transform Infrared Spectroscopy (Bruker Alpha Platinum ATR, 4000–400 cm^{-1}). Surface morphology was examined with a Zeiss EVO 50 Scanning electron microscope at 20 kV. Drug release was monitored by UV–Visible spectrophotometry Hitachi U-2910 spectrophotometer (Tokyo, Japan) at 272 nm using phosphate buffer media at physiological pH.

3. Results and Discussion

3.1. Latex characterization

Protein content was quantified using the Kjeldahl method; dry rubber content, total solid content and ash content were evaluated using the method of Standard African Rubber Manual 1998 and pH was obtained using a calibrated pH meter.

Table 2. Natural rubber latex characterization.

Characterization	Result (%)
Protein content before centrifugation	1.274
Protein content after centrifugation	0.175
Dry rubber content (DRC)	27.238
Total solid content (TSC)	7.149
Ash content (AS)	0.006

According to Table 2, the latex's pH was found to be 5.6. This is within the skin's pH range of 5.5-5.7 indicating that the latex biomembrane should be suitable as a transdermal patch. The protein content of the latex was reduced by 86.26% after centrifugation as shown in the result (from 1.274 to 0.175%). This implies the effective removal of proteins during processing, which is crucial for this application.

3.2. Tensile strength and elongation

Natural rubber latex in general has a good tensile strength and from the results shown in figure 1a, it can be seen that there was steady increase in tensile strength of the biomembrane when loaded with the ampicillin drug and the bioglass. The incorporation of the drug into the latex improved the tensile strength of the latex and also the addition of the bioglass further increased the tensile strength of the biomembrane.

This mechanical improvement is likely due to the drug molecules and bioglass particles acting as reinforcing agents within the polyisoprene network. The drug particles may reduce chain mobility and enhance interchain interactions, while the bioglass functions as inorganic filler that increases matrix stiffness and load-bearing capacity. Similar enhancements in tensile strength have been reported in other polymer–ceramic composites where mineral fillers form physical interlocking points and restrict polymer movement [15]. Therefore, the observed increase in tensile strength can be attributed to the combined effect of reduced chain flexibility and the reinforcing role of the bioglass particles [16].

Figure 1b shows the elongation nature of the biomembranes. Natural Rubber Latex is known to have a good resilience and elastic properties but the result obtained shows a sharp decline in the elongation strength of the biomembranes when the drug and bioglass were incorporated. This can be attributed to the inelastic nature of the drug and the bioglass thereby reducing the resilience and elastic properties of the natural rubber latex [17].

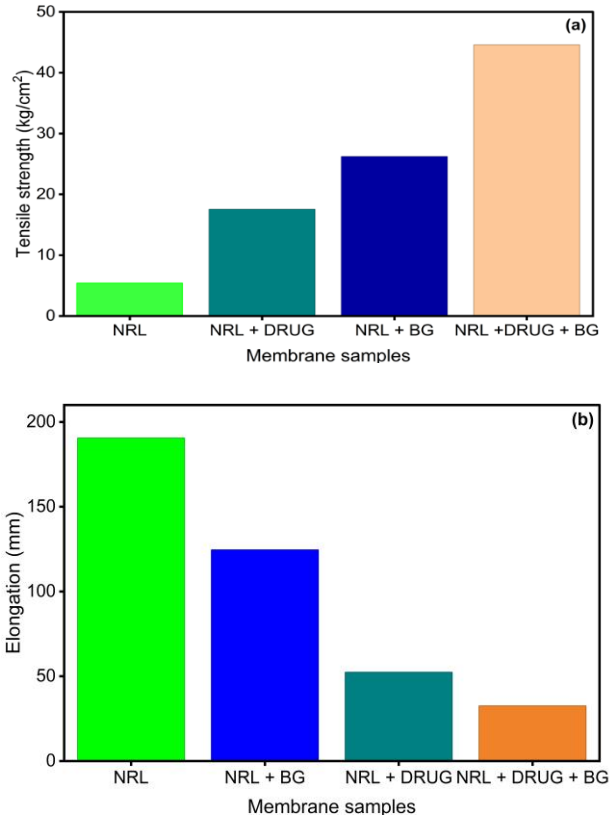

Figure 1. (a) Tensile strength of biomembranes (kg/cm^2) (b) Elongation of biomembranes (mm).

3.3. FTIR

The FTIR spectra for NRL membrane, ampicillin drug sample, NRL + Drug, and NRL + BG + Drug are shown in Fig. 2a, 2b, 2c, and 2d respectively. The FTIR of NRL (Fig. 2a)

shows that the major IR band at 842.4 cm^{-1} is resulting from the polymer, poly (cis-1,4- isoprene). This absorption is mostly important in identifying the NRL molecules and its characteristics. The N-H stretching in the rubber was represented in the band 3295 cm^{-1} to 3444.1 cm^{-1} [18].

In Fig. 2c, the 2967.0 cm^{-1} band represents the C-H stretch and shows the stable presence of the ampicillin drug in the latex membrane. The N-H stretch was observed in the band 3444.1 cm^{-1} and shows the presence of an amine. The band 1766.8 cm^{-1} resulted from the C=O anhydride present in the drug (these bands were present in the drug spectrum as shown in Fig. 2b [19].

only acted as a carrier of the drug and each of them still maintained their characteristics [21].

3.4. SEM

The SEM micrographs of the NRL, NRL–ampicillin, NRL–bioglass, and NRL–bioglass–ampicillin biomembranes revealed differences in surface texture and structural distribution among the samples. The pure NRL membrane exhibited a relatively smooth and uniform surface with minor natural pores characteristic of latex films. Upon incorporation of ampicillin, the membrane surface showed slight roughening and the appearance of embedded particulate domains, suggesting successful physical

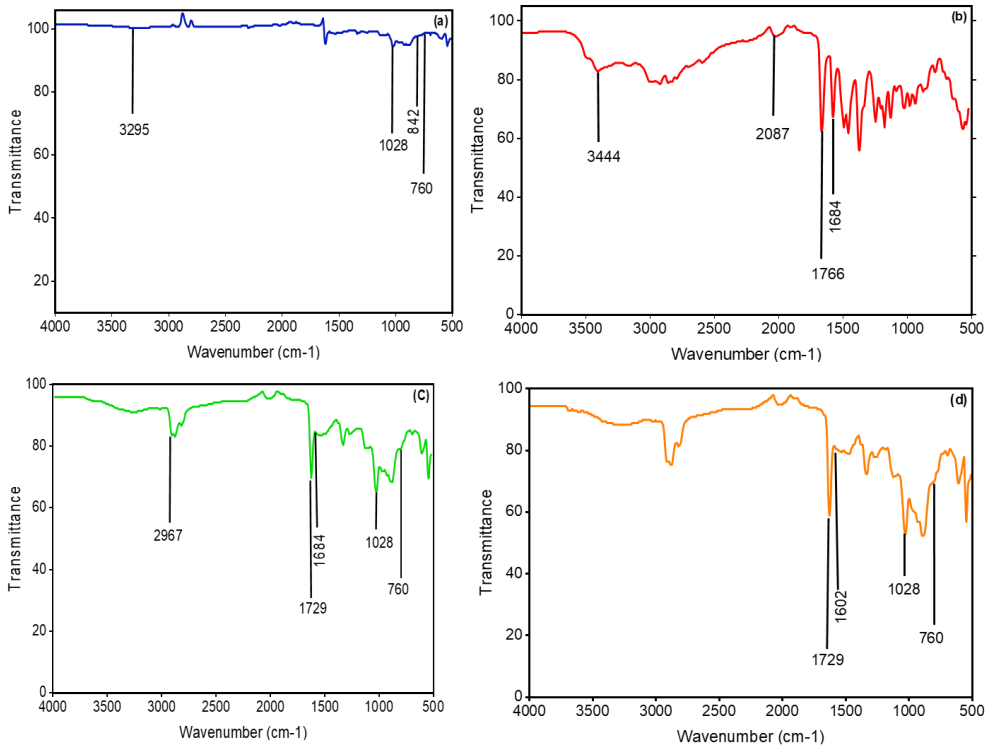

Figure 2. (a) FTIR Spectra of Natural rubber latex membrane, (b) FTIR Spectra of Ampicillin drug sample, (c) FTIR Spectral of Natural rubber latex and Ampicillin drug membrane, (d) FTIR Spectral of Natural rubber latex, Ampicillin drug and Bioglass membrane.

Figure 2d showed the band 1602.8 cm^{-1} which demonstrates the N-H bending primary amine in the bioglass [20]. The NRL absorption peak, on the other hand, doesn't appear to have undergone much of a change in the FTIR spectrum after being loaded with ampicillin and bioglass. When ampicillin was integrated into the latex membrane, its drug intensities somewhat decreased. The ampicillin drug band intensities decreased slightly after it has been incorporated into the latex membrane. This can be as a result of the drug molecules been inserted in the polymer matrix. It was observed that the characteristics band of the NRL, the drug and the bioglass where intact and this implies that despite their compatibilities, there was no major interaction between the polymer matrix as it

entrapment of the drug within the NRL matrix [22]. These discrete drug clusters may contribute to the moderate increase in tensile strength observed in the NRL–ampicillin sample.

For the NRL–bioglass membrane, the SEM images showed more heterogeneous and granular surface features, consistent with the presence of dispersed bioglass particles. The inorganic particles created micro-nodules and increased surface roughness, which aligns with the improved stiffness and reduced elongation at break seen in the mechanical tests [23].

The NRL–bioglass–ampicillin composite exhibited, a combination of drug-associated clusters and bioglass-

induced granules, resulting in a more complex and porous surface morphology. The increased porosity and heterogeneous texture are likely to enhance fluid penetration and facilitate drug diffusion, supporting the higher and more sustained release observed in the drug-release study [24].

showed a broad peak centered around 2θ ≈ 19° – 20°, confirming the amorphous nature of the latex [26].

For the NRL–ampicillin membrane, characteristic crystalline peaks of ampicillin appeared at approximately 2θ = 11.4°, 14.8°, 18.5°, and 22.7°, consistent with

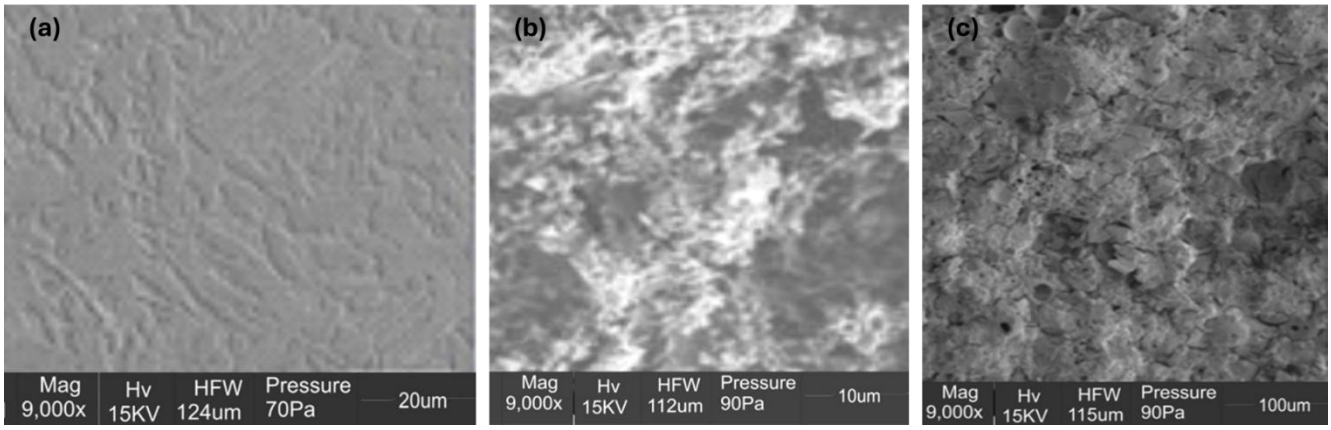

Figure 3. micrography of (a) natural rubber latex membrane, (b) natural rubber latex (NRL) and drug membrane, (c) NRL, drug, and bioglass membrane.

Overall, the morphological differences observed through SEM reflect the distinct contributions of ampicillin and bioglass to the structural architecture of the membranes, helping to explain the corresponding variations in mechanical properties and drug-release behavior. Figures 3a, 3b, and 3c reveal the images produced from the pure NRL, the NRL + drug, and the NRL + BG + drug membranes respectively. It is evident that a reasonable amount of drug is found on the membrane's surfaces forming solid aggregates. Additionally, Fig. 3c demonstrated an appropriate solid fusion and how well the drug and bioglass are mixed into the latex and on its surface when compared to Figure 3b with less compatibility.

3.5. XRD

Ampicillin crystalline nature has been well established in previous literature. Ampicillin exhibits distinct diffraction peaks characteristic of a crystalline solid, as demonstrated through XRD. Multiple studies have confirmed that commercial ampicillin exists in defined crystalline polymorphs, including Form I, Form II, and the trihydrate form, all showing sharp and well-resolved diffraction peaks [25].

The XRD patterns of the NRL, NRL–ampicillin, NRL–bioglass, and NRL–bioglass–ampicillin composites were analyzed to evaluate the crystalline contributions of both the drug and the bioglass within the latex matrix. Natural rubber latex typically exhibits a broad amorphous halo due to its predominantly amorphous cis-1,4-polyisoprene structure. In the pure NRL sample, the diffraction pattern

previously reported diffraction patterns of ampicillin [27]. These peaks were present but reduced in intensity, suggesting partial loss of crystallinity upon dispersion within the latex matrix. XRD patterns of the pure NRL membrane and the loaded membranes (NRL + drug, NRL + bioactive glass, and NRL + drug + bioactive glass) show very similar diffraction profiles, characterized by broad diffuse features and the absence of sharp Bragg peaks. Curing and film-formation process also contributes to this behavior. During curing, the polymer chains rearrange and lock the drug and bioactive glass particles within the matrix, preventing phase separation or crystallization. This results in a homogeneous amorphous composite structure, which is commonly observed in rubber-based and polymer-based delivery systems [28,29].

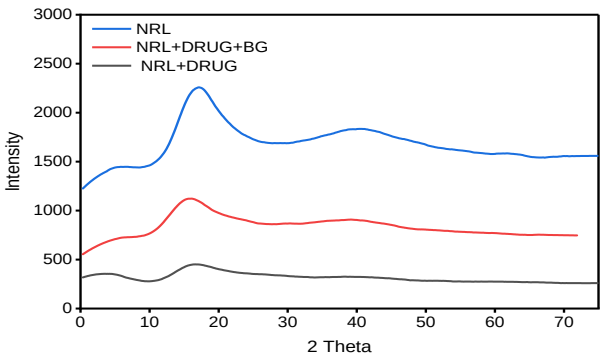

Figure 4. XRD spectrum o XRD spectra of biomembranes.

Therefore, the similarity of the XRD patterns across all membranes indicates that NRL remains the dominant structural phase, while the drug and bioactive glass are

well incorporated and well dispersed within the matrix without forming separate crystalline domains. In the context of drug-delivery applications, this is a desirable outcome, as amorphous systems generally promote improved molecular dispersion, stability, and controlled drug release. The XRD results thus confirm the successful fabrication of the loaded membranes and their suitability as polymer-based drug-delivery platforms

3.6. Drug release analysis using UV spectrophotometer

The drug-release profiles of the NRL–ampicillin and NRL–bioglass–ampicillin membranes were evaluated in buffer solutions of pH 5.5 and 7.4 to simulate different physiological environments.The pH 5.5 buffer represents the slightly acidic conditions typically found on the skin surface and in certain wound environments, while pH 7.4 corresponds to normal physiological pH, such as interstitial fluid and systemic circulation. Using both media allows assessment of how the membranes perform in conditions relevant to transdermal and wound-healing applications.

Figure 5a-b show the release of the ampicillin drug as a function of time. A reasonable amountt of drug was released into the buffer solution at the early hours and this can be attributed to the drug been adsorbed at the surface of the membrane. This much release at the early hours is referred to as “burst release”. A substantial amount of drug was released during the initial hours, which can be attributed to drug molecules adsorbed on or near the membrane surface. This rapid initial release is known as burst release, a typical phenomenon observed in polymer-based drug-delivery systems [30].

lower pH, partial protonation of the drug reduces its solubility and limits release. Additionally, bioglass undergoes faster ion-exchange reactions in neutral media, generating a more hydrated and porous microenvironment that facilitates drug diffusion [32].

The morphology and structure of the composite membranes also influence the release behavior. SEM results revealed that the NRL–bioglass–ampicillin sample possessed a more heterogeneous and porous surface, which increases fluid penetration and accelerates drug release [33]. XRD analysis showed reduced crystallinity of ampicillin within the composite, a factor that generally improves dissolution and release rates [34]. The tensile-strength results further support this observation, as the addition of bioglass produced a stiffer and more open microstructure that enables easier migration of the drug through the matrix.

Overall, the results indicate that the combined effects of drug ionization at physiological pH, bioglass-induced porosity, reduced drug crystallinity, and modified mechanical properties contribute to the enhanced and more sustained release observed at pH 7.4 compared to pH 5.5.

The “stable profile” which is the slower release process is due to the ampicillin which has been incorporated into the polymer matrix and diffusing slowly through the pores of the matrix. The pore density of the membrane is a determining factor in the release rate of the drug. This means that the more open the pore density of the membrane, the faster the release of the drugs. It was

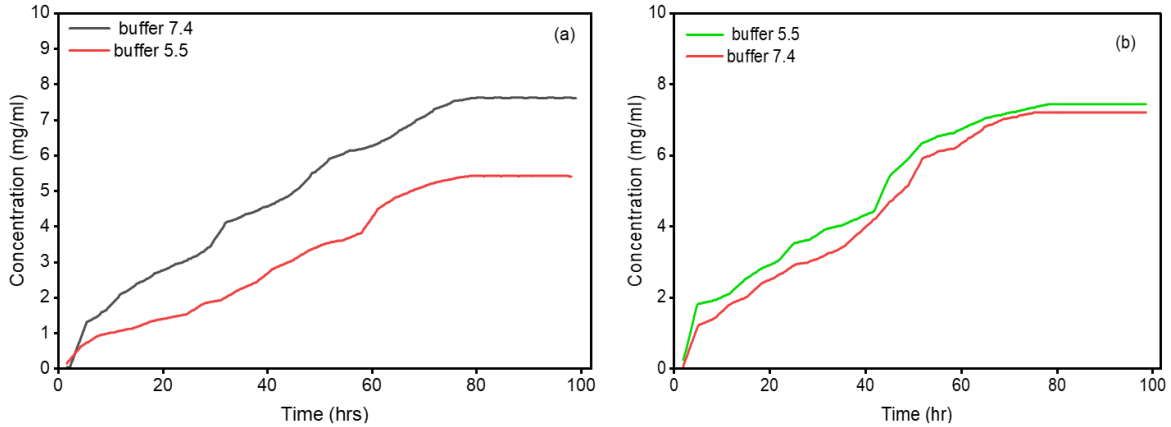

Figure 5. (a) Ampicillin drug release (conc. mg/ml) as a function of time (hour) for NRL+DRUG Biomembrane; (b) Ampicillin drug release (conc. mg/ml) as a function of time for NRL+DRUG + BIOGLASS Biomembrane.

The NRL–bioglass–ampicillin membrane showed higher drug-release activity in pH 7.4 compared to pH 5.5. This increased release at pH 7.4 can be attributed to the greater solubility and ionization of ampicillin at neutral pH, which enhances its diffusion from the polymer matrix [31]. At

observed that the membrane with the bioglass incorporated into it has higher release rate and this can be attributed to the fact that the bioglass aided the opening of the pore matrix of the natural rubber.

4. Conclusion

In conclusion, the study represents a pioneering effort with far-reaching implications in the domain of pharmaceutical advancements. Through a comprehensive investigation into the synergistic potential of natural rubber latex and bioactive glass, this study has unearthed a promising avenue for the development of advanced drug delivery platforms. The in-vitro release exhibited by the composite addresses key challenges in traditional antibiotic therapies, providing a sustained and regulated delivery of ampicillin. This not only contributes to optimizing the therapeutic efficacy of the antibiotic but also presents potential advantages in terms of reducing dosing frequency and improving patient compliance. However, the release profile was found to be pH-dependent, with a higher release rate at pH 7.4 compared to pH 5.5. The release kinetics was best described by the Higuchi model, suggesting that the release mechanism was mainly due to diffusion. Overall, the results of this study suggest that natural rubber latex bioactive composite has the potential to be an effective drug delivery system for ampicillin. Further studies are needed to optimize the formulation and evaluate the in vivo efficacy and safety of the composite.

Author contributions

Idemudia O. Lawrence: Methodology, Project administration; Investigation, Writing – original draft preparation. **Falope Funmilola Yetunde**: Conceptualization, Supervision, Investigation, Visualization; Experimental design, Data curation, Writing – Review and Editing. **Victory Oseosemen Ahuose**: Formal analysis, Validation, Software Sample preparation, Characterization (FTIR, SEM, XRD), Data interpretation, Review and editing. **Aboyewa Jumoke**: Data Curation, Resources, Software. **Ozoemena Happiness**: Resources, Validation.

Conflicts of interest

The authors declare that, there are no conflicts of interest.

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