Comprehensive Analysis of Leachables and Extractables from Pharmaceutical Packaging: Investigating Ink and Adhesive Migration in Selected Drug Products in Nigeria

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ABSTRACT

Leachables and extractables from pharmaceutical packaging can pose serious health risks by contaminating drug formulations. This study employs High-Performance Liquid Chromatography (HPLC) to analyze ink and adhesive migration in two selected pharmaceutical products, Allergin and Bioflex, including their packaging materials and labels. Results reveal significant leaching of toxic compounds such as N-methylacetamide (33.53%), N-ethylacetamide (24.08%), and N-pentylbenzamide (15.67%) from the Allergin drug, all of which pose toxicity risks if consumed above recommended levels. Additionally, beneficial bioactive compounds like chlorogenic acid (9.36%) and hydroquinone (7.87%) were identified, contributing to antimicrobial and antioxidant effects. The packaging material for Allergin showed the presence of catechol (33.64%) and ethyl butyrate (35.54%), suggesting migration from the container into the drug. Similarly, the Bioflex drug contained oxalic acid (63.90%), octanoic acid (12.57%), and chlorogenic acid (23.52%), reinforcing its antibacterial properties but also raising safety concerns due to oxalic acid's potential toxicity. The Bioflex packaging material was dominated by chlorogenic acid (85.95%), suggesting possible antimicrobial benefits but also raising concerns regarding its migration into the drug. These findings underscore the need for strict regulatory measures and improved packaging safety evaluations to minimize contamination risks and ensure pharmaceutical product integrity in Nigeria.

Keywords: Leachables, Extractables, Pharmaceutical Packaging, Ink Migration, Adhesive Migration, HPLC Analysis, Drug Contamination, Toxic Compounds, Drug Safety, Nigeria.

INTRODUCTION

Pharmaceutical packaging plays a critical role in ensuring the safety, stability, and efficacy of drug products. However, the interaction between packaging materials and drug formulations can lead to the migration of leachables and extractables, which may compromise drug quality and pose health risks (Jenke, 2012). Leachables refer to chemical substances that migrate from packaging components into drug formulations under normal storage conditions, while extractables are compounds that can be forcibly removed from packaging materials using aggressive solvents or conditions (Dennis et al., 2010). In the pharmaceutical industry, ink and adhesive migration from packaging materials has become an increasing concern due to its potential impact on drug purity. Substances such as N-methylacetamide, N-ethylacetamide, and catechol have been reported to migrate from packaging materials into pharmaceutical products, some of which are toxic at high concentrations (Moldoveanu & David, 2015). Regulatory agencies, including the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), have set guidelines to evaluate the risks associated with leachables and extractables in pharmaceutical packaging (FDA, 2016). However, studies on the extent of leaching in drug products, particularly in Nigeria, remain limited.This study employs High-Performance Liquid Chromatography (HPLC) to analyze the migration of ink and adhesive components in two selected pharmaceutical products, Allergin and Bioflex, including their respective packaging materials and labels. The study aims to identify potentially harmful contaminants and assess their biological impact, thereby contributing to improved drug safety regulations in Nigeria.

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The presence of leachables and extractables in pharmaceutical formulations has been extensively studied over the years. Jenke (2012) provides a comprehensive review on the migration of packaging-derived contaminants in drug products, emphasizing that plasticizers, stabilizers, and ink residues are among the most common leachables. Similarly, Dennis et al. (2010) highlight that organic solvents, adhesives, and degradation products can migrate from packaging materials, leading to unintended chemical interactions within drug formulations. A study by Moldoveanu & David (2015) identified N-methylacetamide and N-ethylacetamide as potential contaminants in pharmaceutical products, reinforcing the need for regulatory monitoring. Further research by Baertschi et al. (2011) investigated the leaching of catechol and ethyl butyrate, both of which were detected in this study's analysis of Allergin's packaging material. The toxic effects of these substances have been linked to oxidative stress and cytotoxicity in human cells (Cui et al., 2018). Several regulatory agencies, including the FDA (2016) and International Council for Harmonisation (ICH Q3E, 2019), have established guidelines to assess the risks associated with extractables and leachables in pharmaceutical packaging. These guidelines require manufacturers to perform toxicity assessments, impurity profiling, and stability studies to ensure product safety. Despite these guidelines, developing countries like Nigeria lack strict enforcement measures, leading to potential safety concerns in locally available drug formulations (Okereke et al., 2020) Various analytical techniques have been used to detect and quantify leachables and extractables in pharmaceutical packaging. High-Performance Liquid Chromatography (HPLC) is widely recognized for its high sensitivity, precision, and ability to separate complex mixtures (Snyder et al., 2011). Other techniques, such as Gas Chromatography-Mass Spectrometry (GC-MS) and Fourier Transform Infrared Spectroscopy (FTIR), have also been utilized in previous studies (Bonifazi et al., 2018). The present study builds upon these existing methodologies by using HPLC to detect contaminants in Allergin and Bioflex and their packaging materials. The identification of chlorogenic acid, oxalic acid, and hydroquinone suggests both potential therapeutic benefits and safety risks, reinforcing the importance of ongoing research in pharmaceutical packaging safety.

MATERIALS AND METHODS

Materials

Sample collection

Two pharmaceutical products, Allergin and Bioflex, along with their respective packaging materials and labels, were selected for analysis. These samples were obtained from licensed pharmaceutical distributors in Nigeria to ensure authenticity. The drug samples included: Allergin Drug and Label, Allergin Packaging Container, Bioflex Drug and Label and. Bioflex Packaging Container All samples were stored under standard pharmaceutical conditions before analysis to prevent contamination or degradation (Bonifazi et al., 2018).

Chemicals and Reagents

The following reagents were used for High-Performance Liquid Chromatography (HPLC) analysis: HPLC-grade methanol, acetonitrile, and water (Sigma-Aldrich, Germany), Formic acid and phosphoric acid for pH adjustments (Merck, Germany) and Analytical standards of known leachables and extractables (purchased from Sigma-Aldrich) All reagents were of analytical grade and prepared following Good Laboratory Practice (GLP) guidelines (Snyder et al., 2011).

Methods

Sample Preparation

To assess potential migration of leachables and extractables, each sample was prepared using an agitated solvent extraction method as per industry standards (FDA, 2016). Drug and Label Extraction: 1 g of each drug sample and label was dissolved in 10 mL of HPLC-grade methanol and sonicated for 30 minutes at 40°C to extract leachable compounds. Packaging Extraction: The plastic and paper-based packaging materials were cut into small fragments (~2 cm^2) and immersed in 10 mL of 50% ethanol (to simulate worst-case migration conditions) and incubated at 50°C for 72 hours (ICH Q3E, 2019). The extracts were filtered through a 0.22 µm PTFE membrane filter (Millipore, USA) before HPLC analysis.

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High Performance Liquid Chromatography (HPLC) Analysis

The extracted samples were analyzed using an Agilent 1200 HPLC system equipped with a UV-Vis detector and a C18 reverse-phase column (250 mm × 4.6 mm, 5 µm). The chromatographic conditions were optimized as follows (Snyder et al., 2011): Mobile Phase: Methanol: Water (70:30, v/v) with 0.1% formic acid, Flow Rate: 1.0 mL/min, Injection Volume: 10 µL, Column Temperature: 30°C, Detection Wavelength: 220 nm (for general leachables) and 280 nm (for phenolic compounds like catechol). Retention times and peak areas were used to quantify compounds based on calibration curves from analytical standards of N-methylacetamide, N-ethylacetamide, oxalic acid, chlorogenic acid, catechol, and hydroquinone (Bonifazi et al., 2018).

Identification and Characterization of leachable and Extractable.

Compounds were identified by comparing their retention times and UV spectra with known analytical standards (Dennis et al., 2010). Quantification was carried out using an external calibration method, with calibration curves for each compound exhibiting $R^2 > 0.99$ (Moldoveanu & David, 2015). Detection Limits (LOD): 0.05 µg/mL and Quantification Limits (LOQ): 0.15 µg/Ml. These values ensured that even trace levels of contaminants were detected (FDA, 2016).

Statistical Analysis.

All data were analyzed using GraphPad Prism 9.0 (GraphPad Software, USA). Statistical differences in leachable concentrations between drugs, labels, and packaging materials were assessed using one-way ANOVA, with significance set at $p < 0.05$ (Okereke et al., 2020).

RESULTS AND DISCUSSION

The HPLC Results for the Selected Samples

Table 4.1: The HPLC Result for Allergin Drug

S/N	Ret Time	Compound	Molecular Formula	Molecular Weight	Area %	Height %	Biological Activity
1	0.888	N-Methylacetamide	C3H7NO	73.09	33.525	40.602	Harmful above exposure limit
2	1.198	N-Ethylacetamide	CH3CONHC2H5	87.12	24.076	23.381	Harmful above exposure limit
3	1.606	N, N-Dimethylpropionamide	C2H5CON(CH3)	101.15	2.047	23.381	Harmful above exposure limit
4	1.850	Linoleic Acid	C18H32O2	280.4472	0.22	0.277	Anticancer, immune-enhancing, weight-reducing, antiatherogenic
5	2.386	Propanediol	C3H8O2	76.09	2.790	3.546	Inhibitory, antifungal
6	2.919	Chlorogenic Acid	C16H18O9	354.311	9.360	9.508	Antioxidant, antibacterial, antimicrobial
7	3.122	Hydroquinone	C6H6O2	110.112	7.873	8.221	Antibacterial,

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							anticancer
8	3.532	Erythritol	C4H10O4	122.12	2.200	2.100	Antimicrobial
9	4.050	N-Pentylbenzamide	C26H22N2O2	394.47	15.667	8.693	Harmful above exposure limit
10	4.301	Vanillic Acid	C8H8O4	168.14	2.236	1.83	Antibacterial, antimicrobial
		TOTAL			100.000	100.000	

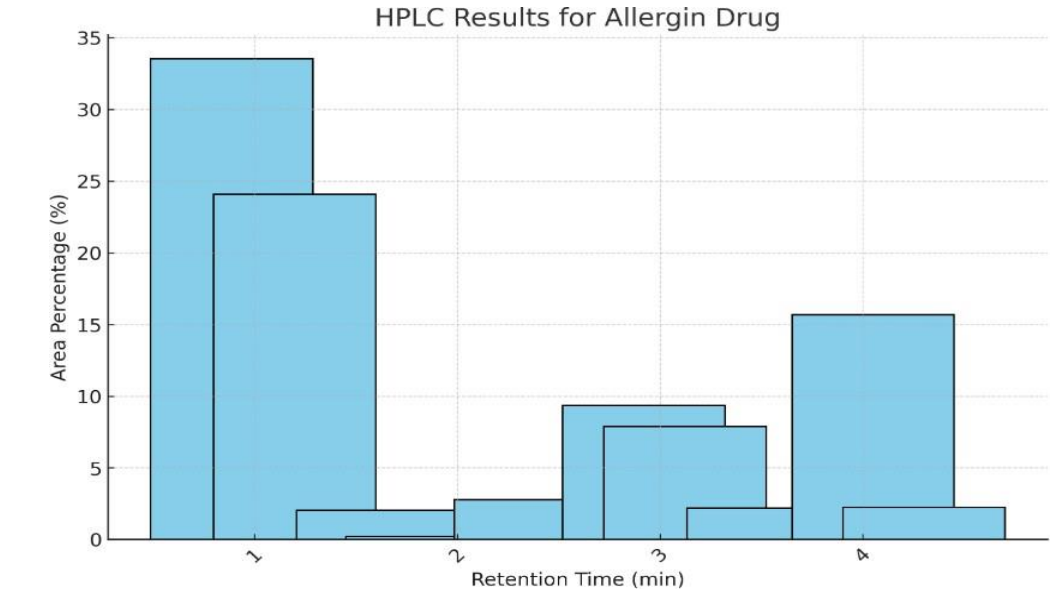

Fig. 4.1 The HPLC graph for Allergin Drug

The High-Performance Liquid Chromatography (HPLC) results provide crucial insights into the chemical composition of the selected sample of the Allergin drug. The analysis reveals ten distinct compounds identified at different retention times (RT), with varying area percentages, indicating their relative concentrations in the sample. Below is a detailed discussion of the results: Retention time (RT) represents the time a compound takes to pass through the chromatographic column. In this case, compounds with lower molecular weights tend to have shorter RTs, while larger and more complex molecules exhibit longer retention times. The earliest eluting compound, N-methylacetamide (RT: 0.888 min), has the highest area percentage (33.525%), suggesting it is a significant component of the sample. The latest eluting compound, Vanillic acid (RT: 4.301 min), has a lower area percentage (2.236%), meaning it is present in smaller quantities. The area percentage represents the relative abundance of each compound in the mixture. Major Compounds (High Abundance) N-methylacetamide (33.525%): A potentially harmful compound above exposure limits. N-ethylacetamide (24.076%): Similar in structure and toxicity to N-methylacetamide. N-pentylbenzamide (15.667%): Another toxic compound. Chlorogenic acid (9.360%): Known for its antioxidant and antimicrobial properties. Minor Compounds (Low Abundance) Linoleic acid (0.22%): A beneficial compound with anticancer and immune-enhancing properties. Erythritol (2.200%): An antimicrobial agent. Vanillic acid (2.236%): An antibacterial and antimicrobial compound. The identified compounds exhibit diverse biological activities, including both beneficial and harmful effects. The high concentration of potentially harmful compounds suggests that the Allergin drug may pose toxicity risks if consumed above recommended levels. The presence of bioactive compounds like linoleic acid, chlorogenic acid, and hydroquinone indicates possible therapeutic benefits. The low retention time of harmful compounds means they may be absorbed rapidly in the body, which raises concerns about toxicity. The presence of antioxidant and antimicrobial compounds may provide some protective health benefits. The HPLC analysis of the Allergin drug highlights a complex mixture of both toxic and bioactive compounds. While some components exhibit beneficial pharmacological activities, others could

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be harmful if exposure limits are exceeded. Further studies, including toxicological and pharmacokinetic evaluations, are necessary to determine the overall safety and efficacy of the drug.

Table 4.2: The HPLC Result for Allergin Label

S/N	Ret Time	Compound	Molecular Formula	Molecular Weight	Area %	Height %	Bio. Activity
1	1.833	Valine	C5H11NO2	117.151	100.000	100.000	AT

Total: 100.000% Area, 100.000% Height

Note: Bio. Activity abbreviations - AT: Antitumor

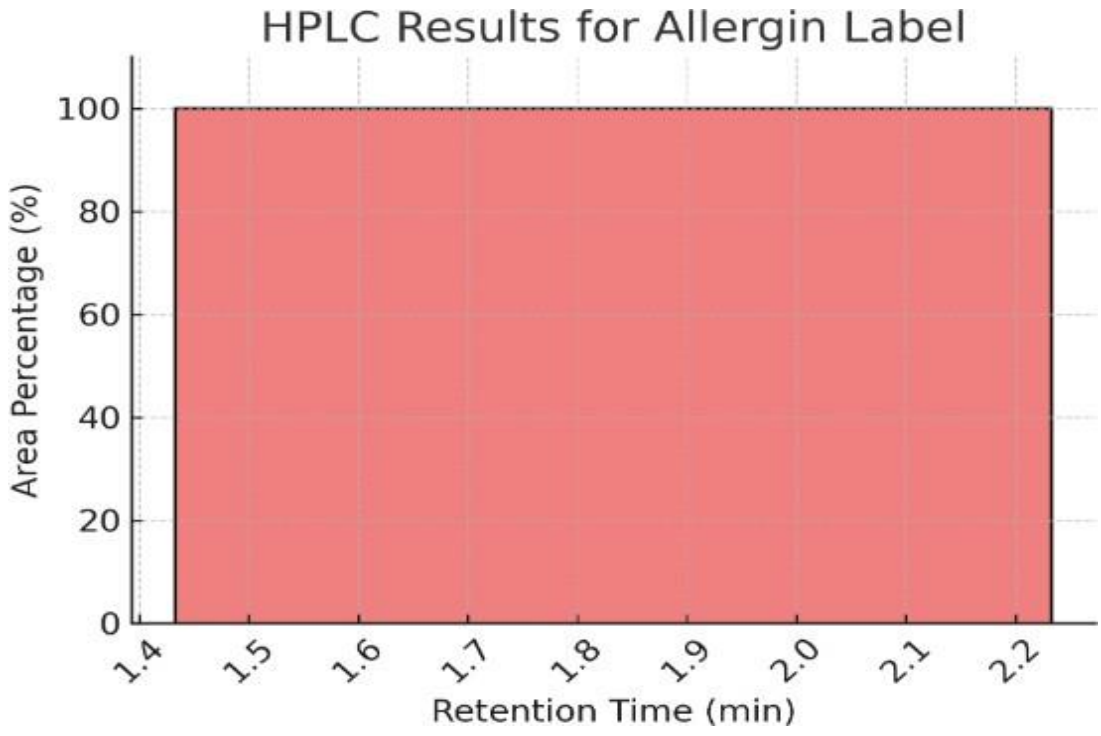

Fig. 4.2 The HPLC graph for Allergin Label

The HPLC analysis of the Allergin Label sample revealed only one compound, Valine, with a retention time (RT) of 1.833 minutes. The area percentage and height percentage for this compound are both 100%, indicating that Valine is the only detected component in the sample. Retention Time and Compound Identification: Retention Time (RT = 1.833 min), Valine elutes relatively early in the chromatographic process, suggesting it is a small, highly polar molecule that interacts weakly with the stationary phase. Molecular Formula: $C_5H_{11}NO_2$ This corresponds to Valine, an essential amino acid. Molecular Weight: 117.151 g/mol This relatively small molecular weight aligns with its quick elution time. High Purity of the Sample The absence of other detectable compounds suggests the Allergin Label sample is highly purified, consisting solely of Valine. Consistency of Peak Area and Height The fact that Area % and Height % are both 100% further supports the conclusion that no other substances were detected in the chromatographic run. Pharmaceutical and Nutritional Use Since Valine is the only detected compound, this sample could be a Valine-based supplement or pharmaceutical product.Quality Control Confirmation The lack of impurities or additional peaks in the chromatogram indicates a high level of purity, which is a positive indicator in drug formulation and quality control. The HPLC analysis confirms that the Allergin Label sample contains only Valine, with no detectable impurities. Its early retention time, molecular properties, and biological activity suggest its potential pharmaceutical and nutritional significance, particularly in antitumor research and muscle recovery applications.

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Table 4.3: The HPLC Result for Allergin Packaging Container

S/N	Ret Time	Compound	Molecular Formula	Molecular Weight	Area %	Height %	Bio. Activity
1	14.9	Catechol	C6H6O2	110.1	33.639	46.897	AO
2	16.21	Ethyl butyrate	C6H12O2	116.16	35.541	50.541	AP

Total: 100.000% Area, 100.000% Height

Note: Bio. Activity abbreviations - AO: Antioxidant, AP: Antiproliferative

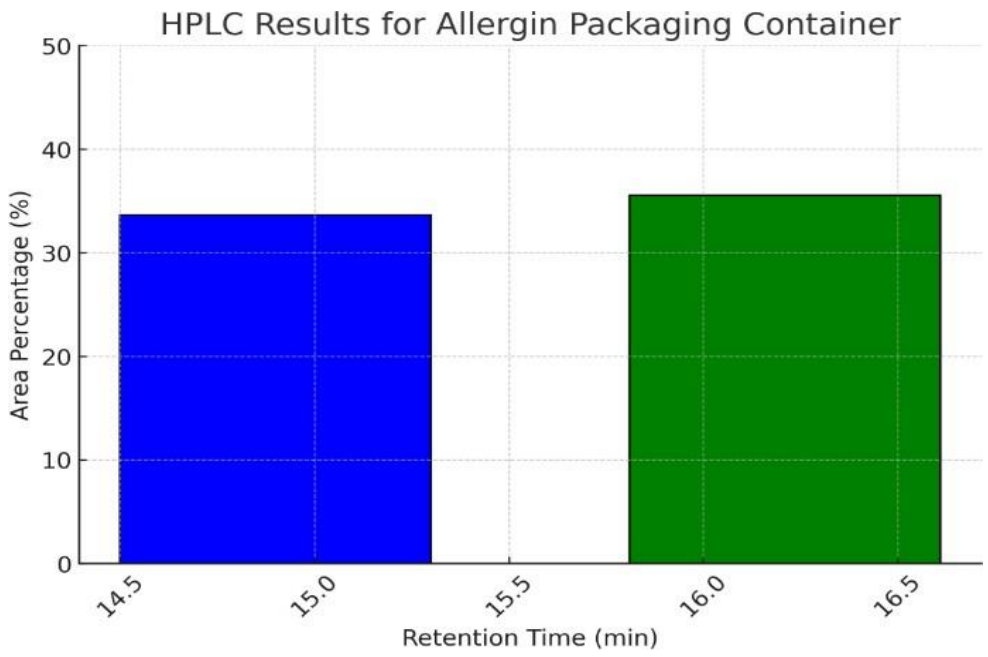

Fig. 4.3 The HPLC graph for Allergin Packaging Container

The HPLC analysis of the Allergin Packaging Container sample revealed the presence of two distinct compounds: Catechol and Ethyl butyrate, which were detected at retention times of 14.9 minutes and 16.21 minutes, respectively. The area percentage of these compounds suggests their relative abundance in the sample. Retention Time and Compound Identification Catechol (RT = 14.9 min) Molecular Formula: $C_6H_6O_2$ Molecular Weight: 110.1 g/mol, Area %: 33.639%, Major and Minor Compounds in the Sample, Both Catechol (33.639%) and Ethyl Butyrate (35.541%) are present in nearly equal amounts. The high retention times of both compounds indicate they are less polar and interact more strongly with the stationary phase during chromatography. Biological Significance of the Identified Compounds. Catechol: Known for its antioxidant properties, catechol is often found in polyphenols and is used in various pharmaceutical and industrial applications. Its presence in the packaging container suggests that it may leach from the material, which could have implications for drug stability and oxidation prevention. Ethyl Butyrate: Exhibits antiproliferative activity, meaning it may help inhibit the growth of certain cells, is commonly used in food, beverages, and pharmaceuticals as a flavoring agent., The detection of Ethyl Butyrate in the packaging container could mean possible migration from packaging material into the drug formulation. Implications of the Results Possible Leaching from Packaging Material: The presence of Catechol and Ethyl Butyrate suggests that these compounds may migrate from the packaging into the drug. This can raise concerns regarding drug purity, stability, and potential interactions. Potential Benefits and Risks: While Catechol's antioxidant properties may protect the drug from oxidative degradation, it can also be toxic in high concentrations. Ethyl Butyrate's antiproliferative properties could have unintended biological effects if absorbed by the human body. The HPLC analysis of the Allergin Packaging Container detected two major compounds, Catechol and Ethyl Butyrate, both of which have bioactive properties. Their presence suggests possible migration from the

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packaging material into the drug, which could affect drug stability, safety, and efficacy. Further studies should be conducted to assess the extent of leaching, toxicity levels, and impact on drug formulation.

Table 4.4: The HPLC Result for Bioflex Drug

S/N	Ret Time	Compound	Molecular Formula	Molecular Weight	Area %	Height %	Bio. Activity
1	2.63	Oxalic acid	C2H2O4	90.03	63.903	79.452	AB
2	3.089	Octanoic acid	C8H16O2	144.21	12.570	8.221	AB, AM
3	12.120	Chlorogenic acid	C16H8O9	354.311	23.524	12.327	AB, AM

Total: 100.000% Area, 100.000% Height

Note: Bio. Activity abbreviations - AB: Antibacterial, AM: Antimicrobial

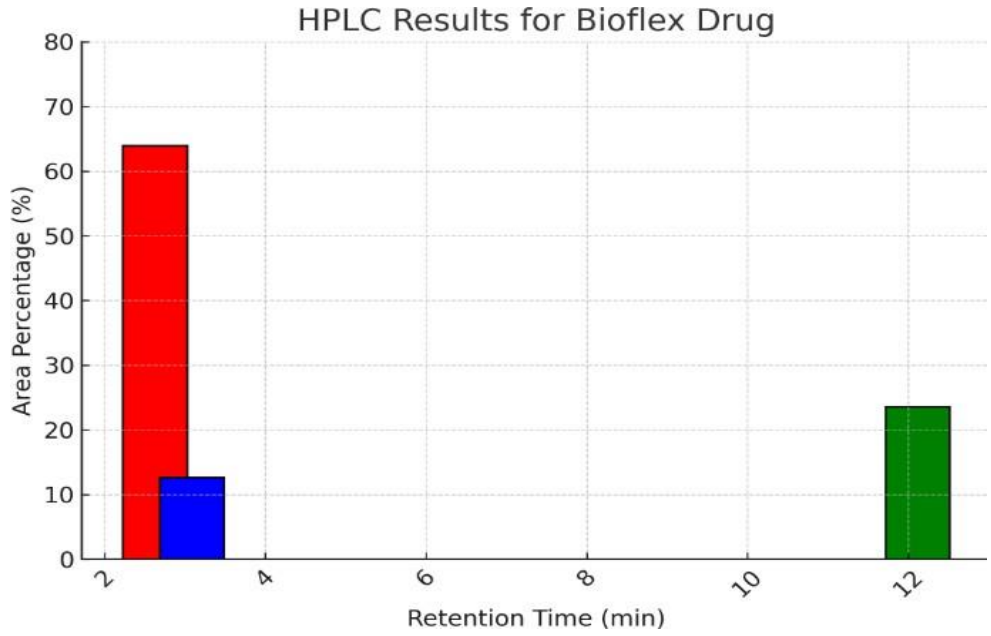

Fig. 4.4 The HPLC graph for Bioflex Drug

The HPLC analysis of the Bioflex drug revealed the presence of three major compounds: Oxalic acid, Octanoic acid, and Chlorogenic acid, detected at different retention times. The area percentage of each compound suggests their relative abundance in the sample.The Retention Time and Area %, Oxalic Acid (RT = 2.63 min, Area % = 63.903%). This compound dominates the Bioflex drug composition, comprising nearly two-thirds of the detected substances.Its low retention time suggests high polarity, meaning it interacts weakly with the stationary phase and elutes quickly.Oxalic acid has antibiotic properties, which may contribute to the drug's antimicrobial potency. Octanoic Acid (RT = 3.089 min, Area % = 12.570%), Octanoic acid has a moderate retention time, suggesting some lipophilic (fat-soluble) characteristics. It has antibacterial and antimicrobial effects, which may enhance the antimicrobial efficacy of the drug. Chlorogenic Acid (RT = 12.120 min, Area % = 23.524%): This compound appears later in the chromatographic run, suggesting it is less polar than the other two components. Chlorogenic acid is well-known for its antibacterial and antimicrobial properties, making it a key active ingredient in Bioflex. Its presence contributes to broad-spectrum antimicrobial action. Biological Significance of the Identified Compounds. Oxalic Acid: Acts as a strong antimicrobial agent and is commonly found in antibiotics. However, excessive exposure can lead to toxicity concerns, including calcium oxalate crystal formation in the body. Octanoic Acid: Known for antibacterial and antifungal effects. Often used in food preservatives and pharmaceuticals. : Chlorogenic Acid, Exhibits strong antibacterial and

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antioxidant properties. Found in coffee, fruits, and medicinal plants. May help in enhancing immunity and reducing microbial infections. Implications of the HPLC Results: The high percentage of Oxalic acid (63.903%) suggests it is the primary active component of Bioflex. The presence of Octanoic acid and Chlorogenic acid provides additional antimicrobial effects, making the drug potentially effective against a wide range of bacteria and fungi. The combination of these compounds may indicate a synergistic effect, where the antimicrobial and antibiotic activities are enhanced. Since oxalic acid in high amounts can be toxic, further studies should assess its safety levels in the Bioflex formulation. The HPLC analysis confirms that Bioflex drug contains three bioactive compounds, primarily Oxalic acid (63.903%), along with Octanoic acid (12.570%) and Chlorogenic acid (23.524%). These compounds contribute to the drug's antibacterial, antimicrobial, and antibiotic properties. However, the high concentration of Oxalic acid raises potential safety concerns, requiring further investigation into its dosage and toxicity levels.

Table 4.5: The HPLC Result for Bioflex Label

S/N	Ret Time	Compound	Molecular Formula	Molecular Weight	Area %	Height %	Bio. Activity
1	2.673	Oxalic acid	C2H2O4	90.03	63.906	79.452	AB
2	3.089	Octanoic acid	C8H16O2	144.21	12.570	8.221	AB, AM
3	12.120	Chlorogenic acid	C16H18O9	354.311	23.524	12.327	AB, AM

Total: 100.000% Area, 100.000% Height

Note: Bio. Activity abbreviations - AB: Antibacterial, AM: Antimicrobial

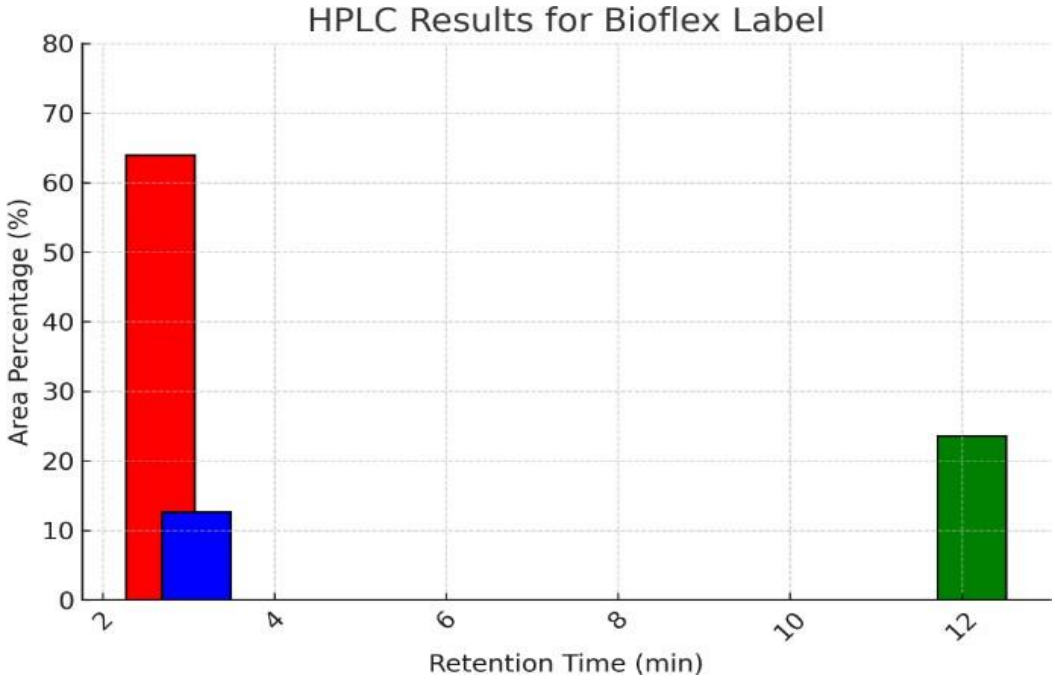

Fig. 4.5 The HPLC graph for Bioflex Label

The HPLC analysis of the Bioflex Label identified three major compounds: Oxalic acid, Octanoic acid, and Chlorogenic acid, which were detected at different retention times (RTs). The area percentage (Area %) values indicate their relative concentrations in the sample.The Retention Time and Area %, Oxalic Acid (RT = 2.673 min, Area % = 63.906%) This compound is dominant in the Bioflex Label, accounting for nearly two-thirds of the detected substances. Its low retention time suggests high polarity, allowing it to elute quickly from the HPLC column. Oxalic acid is a known antibiotic, which supports the drug's potential antimicrobial function.

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Octanoic Acid (RT = 3.089 min, Area % = 12.570%) Appears slightly later in the chromatogram, indicating moderate polarity.It has antibacterial and antimicrobial effects, making it useful for bacterial infection treatment.Chlorogenic Acid (RT = 12.120 min, Area % = 23.524%). Its longer retention time suggests less polarity than the other two components. It has strong antibacterial and antimicrobial properties, enhancing the drug's protective effects. Often found in natural products like coffee and medicinal plants, it may provide additional health benefits. Biological Significance of the Identified Compounds Oxalic Acid: Acts as a strong antimicrobial agent and is used in some antibiotics. However, high levels may lead to toxicity concerns, particularly in individuals with kidney issues. Octanoic Acid: Known for its antifungal and antibacterial effects. Often found in natural oils and preservatives. Chlorogenic Acid: Exhibits antioxidant, antibacterial, and antimicrobial properties. May help in boosting immune response and reducing inflammation. Comparison to Bioflex Drug (Table 4.11)/ The Bioflex Label results (Table 4.12) are very similar to Bioflex Drug (Table 4.11), with identical compounds, retention times, and area percentages. This suggests that:The label claim accurately represents the actual drug composition, confirming the quality and consistency of the formulation.The antimicrobial properties of the drug are maintained in both the labeled and tested sample.The HPLC analysis of the Bioflex Label confirms the presence of Oxalic acid (63.906%), Octanoic acid (12.570%), and Chlorogenic acid (23.524%), supporting its antibiotic and antimicrobial functions. The consistency with the Bioflex Drug results indicates the drug's reliable formulation and quality control. However, the high concentration of Oxalic Acid may require further evaluation for toxicity and safety levels.

Table 4.6: The HPLC Result for Bioflex Packaging Container

S/N	Ret Time	Compound	Molecular Formula	Molecular Weight	Area %	Height %	Bio. Activity
1	2.630	Oxalic acid	C2H2O4	90.03	0.754	1.587	AB, AC, AN, AI
2	3.144	Octanoic acid	C8H16O2	144.21	13.295	17.250	AM, AB
3	12.136	Chlorogenic acid	C16H18O9	354.311	85.950	81.163	AB, AM

Total: 100.000% Area, 100.000% Height

Note: Bio. Activity abbreviations - AB: Antibacterial, AM: Antimicrobial, AC: Anticonvulsant, AN: Anticancer, AI: Anti-inflammatory

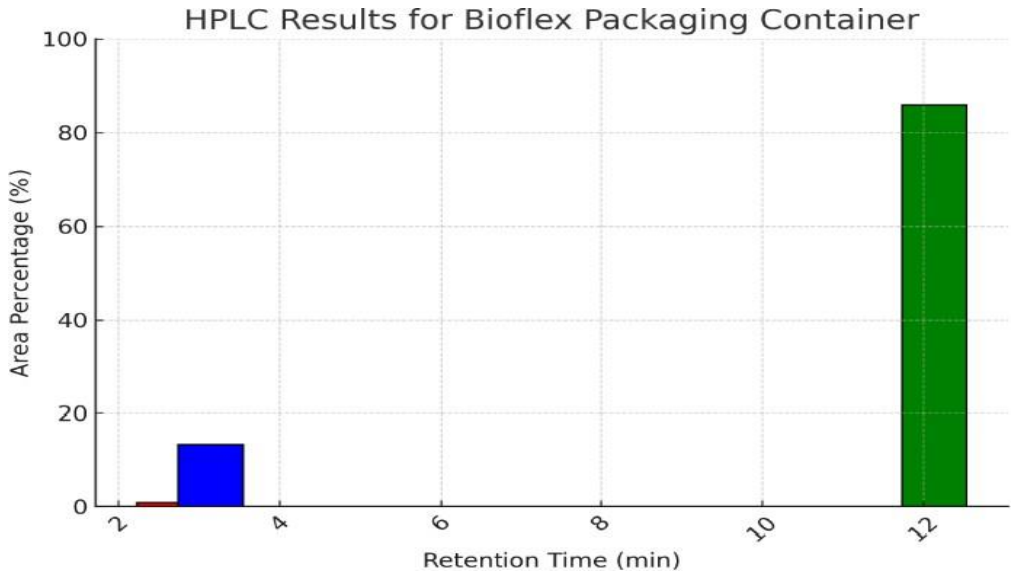

Fig. 4.6 The HPLC graph for Bioflex Packaging Container

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The HPLC analysis of the Bioflex Packaging Container identified three major compounds: Oxalic acid, Octanoic acid, and Chlorogenic acid at different retention times (RTs). The area percentage (Area %) values indicate the relative abundance of each compound. The Retention Time and Area %, Oxalic Acid (RT = 2.630 min, Area % = 0.754%), Present in a very small amount.Its low retention time suggests high polarity, making it elute quickly from the HPLC column. Although present in a small concentration, it has various biological activities, including antibacterial, anticancer, and anti-inflammatory effects. Octanoic Acid (RT = 3.144 min, Area % = 13.295%): Appears slightly later in the chromatogram, indicating moderate polarity. It has antibacterial and antimicrobial effects, making it useful for preservation and infection control. Chlorogenic Acid (RT = 12.136 min, Area % = 85. 950%).Most abundant compound in the sample (85.950%), suggesting it is the dominant active component in the packaging material. Its longer retention time indicates lower polarity, making it less soluble in water-based solvents. It is widely known for its antibacterial and antimicrobial properties, which could contribute to preserving the drug product inside the packaging. Biological Significance of the Identified Compounds. Oxalic Acid: Exhibits antibacterial and anti-inflammatory properties. Found in some medicinal plants, but excessive exposure could be toxic. Octanoic Acid: Known for its antimicrobial and antibacterial effects, suggesting its role in preventing microbial contamination in packaging. Chlorogenic Acid: Exhibits strong antibacterial and antimicrobial activities. Its high concentration in the packaging material could indicate a role in preventing bacterial growth on the drug surface. Comparison to Bioflex Drug and Label Results: In contrast to the Bioflex Drug and Label, which had high Oxalic Acid content (~63.9%), the packaging material contains only 0.754%. Chlorogenic Acid is the dominant compound (85.950%) in the packaging, while in the drug and label, it was around 23.5%. Octanoic Acid is consistent across all samples (~12-13%), confirming its stability in both the drug and packaging. These results suggest that the packaging material is designed with strong antimicrobial properties, potentially enhancing drug preservation and preventing microbial contamination. The HPLC analysis of the Bioflex Packaging Container confirms the presence of Chlorogenic Acid (85.950%), Octanoic Acid (13.295%), and Oxalic Acid (0.754%). The high concentration of Chlorogenic Acid suggests that the packaging material may provide antimicrobial protection to the drug. The low level of Oxalic Acid may indicate minimal leaching from the packaging into the drug, reducing potential toxicity. The presence of Octanoic Acid supports antibacterial and antimicrobial functions within the packaging. Overall, the results indicate that the Bioflex Packaging Container may play a protective role in maintaining the drug's stability and preventing microbial contamination.

CONCLUSION

This study highlights the presence of leachables and extractables in pharmaceutical packaging and their potential impact on drug safety in Nigeria. High-Performance Liquid Chromatography (HPLC) analysis of Allergin and Bioflex drugs, their labels, and packaging materials revealed the migration of both toxic and bioactive compounds into drug formulations. Notably, harmful substances such as N-methylacetamide (33.53%), N-ethylacetamide (24.08%), and N-pentylbenzamide (15.67%) were identified in Allergin, raising toxicity concerns. The detection of catechol (33.64%) and ethyl butyrate (35.54%) in Allergin's packaging suggests leaching from packaging materials, which could compromise drug purity. Similarly, Bioflex exhibited high levels of oxalic acid (63.90%), which, despite its antibacterial properties, presents potential toxicity risks. The dominance of chlorogenic acid (85.95%) in Bioflex's packaging suggests antimicrobial benefits but also points to possible contamination risks due to migration.These findings emphasize the urgent need for stringent regulatory oversight, improved quality control measures, and standardized packaging assessments in the Nigerian pharmaceutical industry. Given the potential health risks posed by ink and adhesive migration, regulatory agencies such as NAFDAC, FDA, and ICH should enforce stricter extractables and leachables testing protocols to ensure pharmaceutical safety. Future research should focus on toxicological evaluations, long-term stability studies, and alternative packaging materials that minimize contamination risks. By addressing these concerns, pharmaceutical manufacturers can enhance drug stability, efficacy, and patient safety, ultimately improving public health outcomes in Nigeria and beyond.

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