IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

DEVELOPMENT OF CHROMOPHORIC METHOD FOR THE ANALYSIS OF ANTIBIOTIC

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ABSTRACT

This article's goal is to review the content and validity of antibiotics using a variety of spectrophotometric and chromatographic techniques. The present review employed five distinct analytical techniques to examine antibiotics: high-performance liquid chromatography (HPLC), gas chromatography (GC), ultraviolet visible (UV-Vis) spectrophotometer, Fourier transform infrared (FTIR), and liquid chromatography/mass spectrophotometer (LC/MS) methods. The most commonly prescribed medications for bacterial illnesses are antibiotics. Based on a study of multiple research pertaining to antibiotic analysis, HPLC, FTIR, GC, UV-Vis Spectrophotometry, and LC-MS are the commonly used techniques. Because of this antibiotic's sensitivity and volatility under different settings, analysis presents a significant problem.

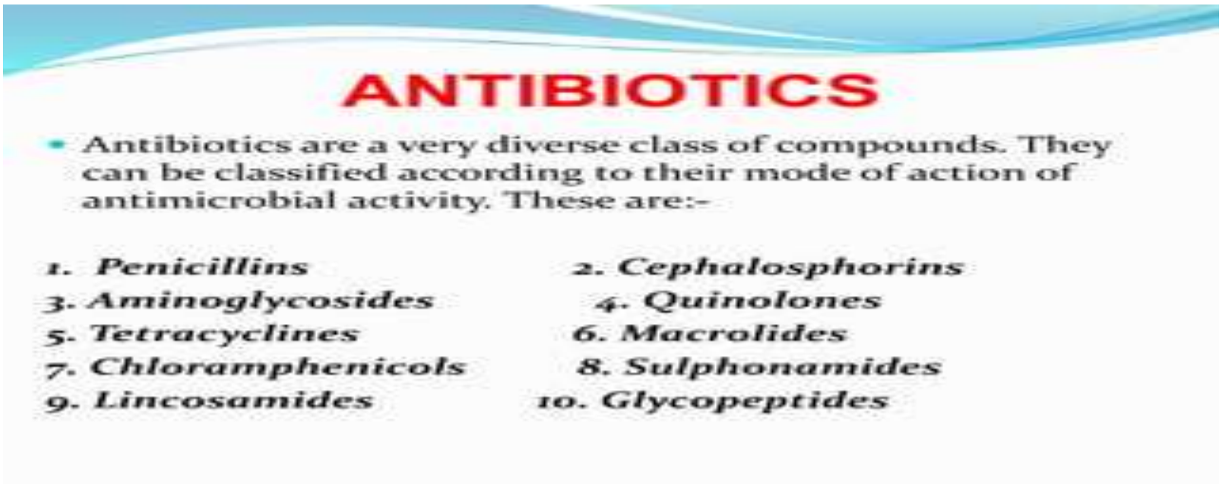
Keywords: Antibiotics, Chromatography, Drugs, Spectrophotometry

INTRODUCTION

The comparatively heavy use of antibiotics poses a hazard to global health and is the cause of many issues, not the least of which is bacterial resistance to antibiotics. It affects not just morbidity and death but also ha266s a strong detrimental effect on the economy and society. Resistance, particularly to Streptococcus pneumoniae, Staphylococcus aureus,and Escherichia coli, started out at the hospital level and progressively spread to the population [1-3].

The most commonly prescribed medications for bacterial illnesses are antibiotics. Numerous studies have revealed that between 40 and 62% of antibiotics are misused or prescribed for conditions for which they are not necessary. Thirty to eighty percent of antibiotic prescriptions were not based on indications, according to studies on the quality of antibiotic use throughout the hospital.

CLASIFICATION OF ANTIBIOTIC

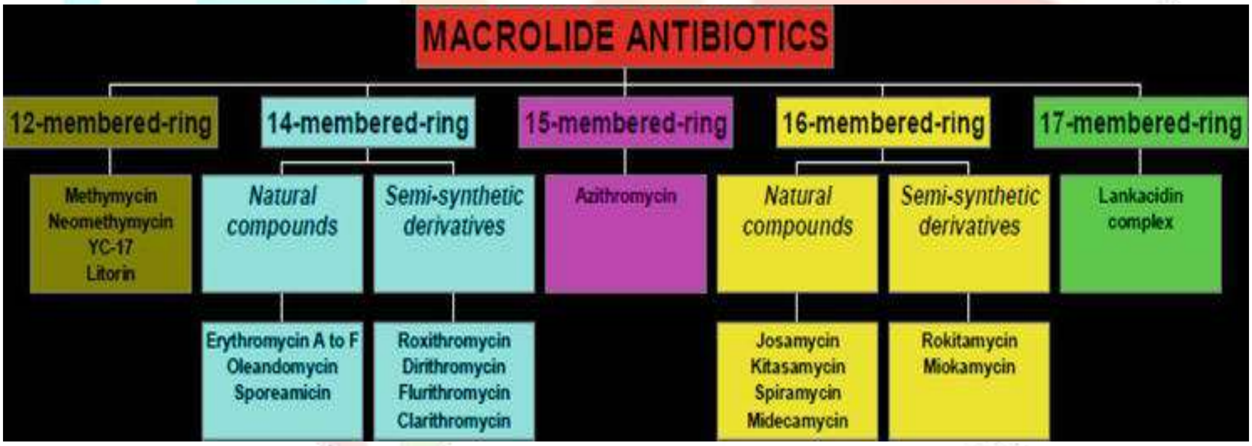


ANTIBIOTICS

- Antibiotics are a very diverse class of compounds. They can be classified according to their mode of action of antimicrobial activity. These are:-

1. Penicillins
2. Cephalosphorins
3. Aminoglycosides
4. Quinolones
5. Tetracyclines
6. Macrolides
7. Chloramphenicols
8. Sulphonamides
9. Lincosamides
10. Glycopeptides

ANTIBIOTIC USED (MACRILIDES)



Azithromycin (An antibiotic)

Antibiotic used to treat various bacterial infections. It works by stopping the growth of bacteria. It's commonly used to treat respiratory tract infections, skin infections, and certain sexually transmitted infections. It's usually taken orally and comes in different forms, like tablets and liquid. It's important to take the full course of medication as prescribed by your doctor. Remember to always consult a healthcare professional for specific medical advice. [2]

High Performance Liquid Chromatography (HPLC):

The most popular technique for analysing cephradine in formulations is HPLC, and various analytical techniques have been reported for analysing cephradine in various pharmaceutical formulations in biological fluids. Although HPLC-UV procedures are quick, they require high temperatures, which can lead to drug thermal deterioration. To prevent this, derivatization is necessary to increase volatility and enhance chromatographic behavior. Therefore, these techniques do not work with antibiotics. Due to the extremely low detection limits of the HPLC-UV approach, it is possible to assess archaeological samples from medicinal medications.

HPLC can be a useful technique in many pharmaceutical research projects since it can be used to analyses and evaluate pharmaceutical, chemical, and high-volatility samples. Numerous antibiotics have ionizable group that is amenable to analysis by ion exchange chromatography techniques. One crucial technique for the isolation and purification of antibiotics is the high-resolving power of HPLC. Numerous HPLC techniques have been documented for the examination of a solitary cephradine in medicinal products. Each of these techniques has a special chromatographic and preparation regimen. Cephradine has been analysed using a number of techniques, including the very sensitive and precise HPLC approach [21–23].

This page goes into more detail about the HPLC technique. These antibiotics' sensitivity and volatility under various settings make analysis difficult.The Zorbax 300SCX Agilent Column Ion Pac column, measuring 5µm by 4.6x250 mm, was employed in the HPLC-UV system to analyse cephradine in capsule form.The accuracy and precision of the results obtained from the HPLC measurements for different concentrations of the cephradine sample are directly impacted by a number of factors, including column type, eluent, concentration, temperature effect, and tR. These factors are part of the analytical performance that was studied for the separation and estimation of the cephradine sample using the HPLC-UV method.The findings demonstrated that Cephradine in capsule form is nearly stable in aqueous medium at room temperature for two to three days.

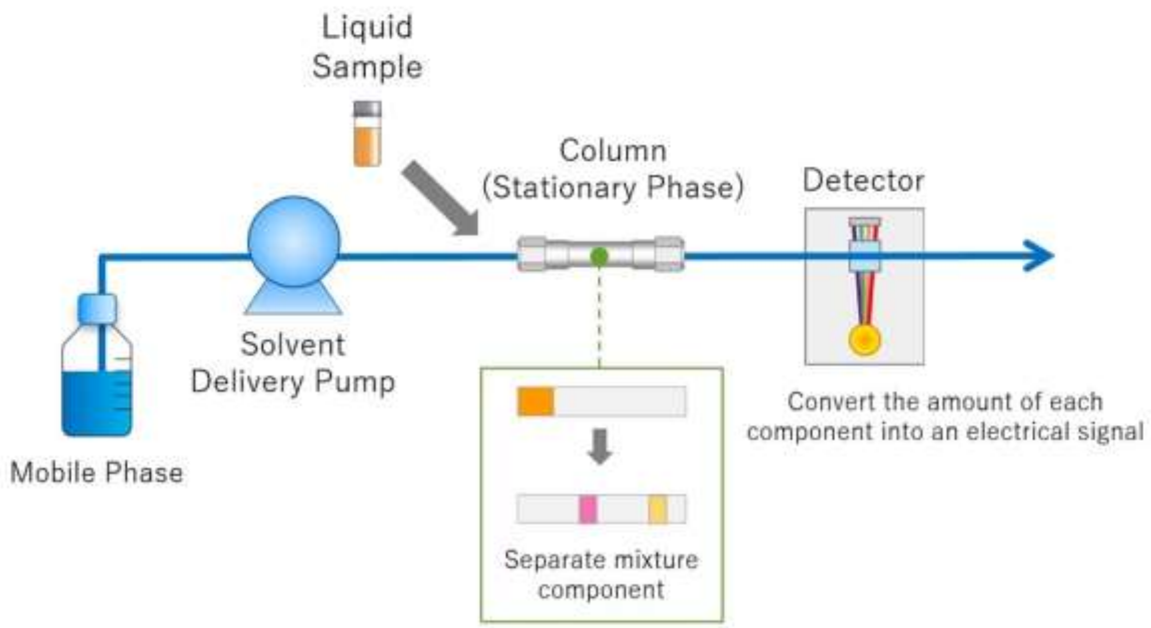


Fig 2-Analytical method by HPLC

Fourier Transform Infrared (FTIR)

Vibrational spectroscopy, another name for infrared spectroscopy, is a common technique in chemical and pharmaceutical study that shows the atoms' vibrations in compounds. Using the FTIR instrument is one way to perform infrared spectroscopy. Samples in liquid, solution, and powder forms can be characterised using the analytical technique known as FTIR. It is not necessary to add dyes or labels to an FTIR analysis in order to visualise the various chemical components present in the sample.FTIR creates an absorbance or transmittance spectrum by simultaneously measuring all wavelengths.

ATR FTIR is one kind of FTIR that can be used to quantify ceftriaxone sodium. ATR is an analytical method based on the bending of light as it travels through various mediums and molecular vibrations. One benefit of FTIR ATR is that it just needs a little sample to be analysed. The spectrum that results from the FTIR study falls between 4000 and 400 cm in wavelength. FTIR-ATR analysis of ceftriaxone sodium can be performed by measuring the peak area of the carbonyl group's resultant spectra, which falls between 1800 and 1700 cm-1 in wavelength [27–30].

An antibiotic of the third generation derived from cephalosporins is ceftriaxone. The HPLC method is typically used for the quantitative analysis of ceftriaxone raw materials in ceftriaxone sodium formulations. Since the HPLC method, in general, requires solvents that are not environmentally friendly, an approach utilising the FTIR-ATR spectroscopic method is conducted. The benefits of this approach include utilising solvents that are safe for the environment, being less expensive, and requiring less time for sample preparation and analysis than the HPLC method. The metrics of linearity, selectivity, precision, accuracy, detection limit, and quantification limit are used to determine the method validation. Based on the validation results, linearity was attained with a quantification limit of 60.68 mg/mL, detection limit of 20.02 mg/mL, and coefficient of determination of 0.9992 in the concentration range of 300-800 mg/mL. So, this approach can be applied as a the Indonesian Pharmacopoeia's recommendations as analytical techniques [31–33].

Gas Chromatography (GC)

The preferred method is static headspace gas chromatography (SH-GC), which has a low detection limit, high sensitivity, good separation capabilities, and straightforward apparatus. Because the static headspace (HS) sampling method can efficiently concentrate volatile analytes from the samplematrix and clearly separate them from it, it has a sensitivity that is more suited than the direct injection method. As a result, this procedure leads to a simpler sample preparation process, lower instrument contamination, and longer GC column life. As far as we are aware, there isn't a validated solid-state GC method that can be used to analyse the residual solvents found in augmentin (also known as amoxicillin) and principen (also known as ampicillin) tablets that are sold in stores. According to the supplier, these pills include three typical class II residual solvents, such as toluene, dichloromethane, and methanol. In A precise measurement of residual solvents is necessary to ensure good manufacturing practices (GMP) and ensure safety.

In this work, we report on the invention and comprehensive validation of a new SH-GC analytical technique for the simultaneous measurement of toluene, dichloromethane, and methanol using a FID detector. A number of criteria, including specificity, linearity, precision, accuracy, limit of detection, limit of quantitation, robustness, and solution stability, were validated in accordance with ICH guidelines. Additionally, the technique is used to find the amount of residual solvents in tablets of ampicillin and amoxicillin that are purchased from the local market. To ensure that they don't go beyond the amount allowed by the ICH rules, these solvents should be approximated and verified. The new technique is straightforward, sensitive, and perhaps beneficial for the quick regular measurement of additional drug compounds' residual solvent levels [34–36]. The development and validation of a straightforward and sensitive static head space gas chromatographic (SH-GC) method with FID has allowed for the simultaneous measurement of residual solvents, such as methanol, dichloromethane, and toluene, in two medicinal medicines, such as ampicillin and amoxicillin. A 30 m long Elite - 5 fused silica capillary column with an inner diameter of 0.32 mm was utilised to achieve the separation.

For every solvent, the established SH-GC technique provided symmetric peak form, acceptable resolution, and a suitable retention duration. For methanol, dichloromethane, and toluene, respectively, concentration ranges of 100–1200, 50–1000, and 50–500 ppm were followed in accordance with Beer’s law. The approach's specificity, linearity, precision, accuracy, limit of detection, limit of quantitation, robustness, and solution were all validated in accordance with the guidelines set out by the International Conference on Harmonization (ICH) steadiness. Additionally, the percent recoveries, relative standard deviation, and degrees of linearity of the calibration curves were resolved. Every validation parameter fell within the permissible bounds. As a result, the established SH-GC approach may find application in regular analysis in any analytical laboratory for the straightforward and quick identification of trace amounts of residual solvents in different pharmaceutical goods [37–40].

Ultraviolet-Visible (UV) Spectrophotometry:

Based on the absorbance value, an existing analysis method utilising ultraviolet-visible spectrophotometry is used. Cefadroxil concentration was measured using an ultraviolet spectrophotometric method with a solvent that had a maximum wavelength of 264 nm and was blended 50:50 with methanol and distilled water. Cefadroxil was shown to be linear in the 10 g/mL to 50 g/mL range, with a correlation value of 0.9999. The following parameters were used to validate this method: robustness, ruggedness, specificity, linearity, accuracy, and precision. A reliable assay for the spectrophotometric analysis of cefadroxil was obtained using this method [41–43].UV s soluble. Cefadroxil's linearity was demonstrated at 8–16 ppm concentrations, as indicated by the area under the curves (AUC) of 0.9974 and 0.9999, respectively, and coefficient values on the absorbance method.

The area under the curve and the absorbance method were used to determine the sample rate for both generic and Cefat-branded cefadroxil capsules. The results showed that the generic cefadroxil capsule had a rate of 99.31% and 98.11%, respectively. By using the absorbance method, it was possible to determine the average yield of percent recovery for both generic and Cefat-branded cefadroxil capsules.

The area under the curve for the generic cefadroxil capsule was 101.91 percent and 98.63 percent, respectively.

The findings of this investigation show that the cefadroxil sample levels utilised in the manufacturing of the capsules satisfy the requirements stated in the Indonesian Pharmacopoeia, Fifth Edition. 90–120 percent in 2014. The absorbance method and the area under the curve are legitimate methods based on the data above [44–46]. spectrophotometry was used in research to create and validate the cefadroxil capsule analysis method. In order to do this study, an analytical solution containing hydrochloric acid (0.1 N HCl) was chosen.

Liquid Chromatography-Mass Spectrometry (LC/MS)

The analytical method known as Liquid Chromatography Mass Spectrometry (LC/MS-MS) combines the mass spectrometry's detection specificity with the physical separation powers of liquid chromatography. A mass spectrometer finds the charged ions in the sample after liquid chromatography separates its constituent parts. The molecular weight, structure, identity, and quantity of certain sample components can all be determined using LC-MS data. Based on how differently a compound interacts with each particle's chemical layers, it is divided into different categories. The ability to analyze a larger variety of components, including heat compounds, is an advantage of LC-MS. proteins, labile, having a large molecular mass or polarity. After that, a unique interface is used to transfer the chromatographic column's elution component to the mass spectrometer.

The idea is to separate analytes according to their polarity. The apparatus is made up of a column that serves as the stationary phase, a specific solution that serves as the mobile phase, and high pressure to force the mobile phase. This will be seen in a spectrum with split peaks as the analyte mixture separates according to its polarity and the speed to reach the detector (retention time) will be variable. The liquid mobile phase pump aid is directed towards the detector via the column. By injection, the sample is added to the mobile phase stream. The components of the mixture separate in the column as a result of variations in the strength of the interaction between the solution and the phase that is stationary. The first solution to exit the column is the one that interacts with the stationary phase less strongly. Conversely, a powerful solution interacts with the stationary phase to cause the solution to exit the column, where it is subsequently picked up by the detector and captured on a chromatogram [47–50].

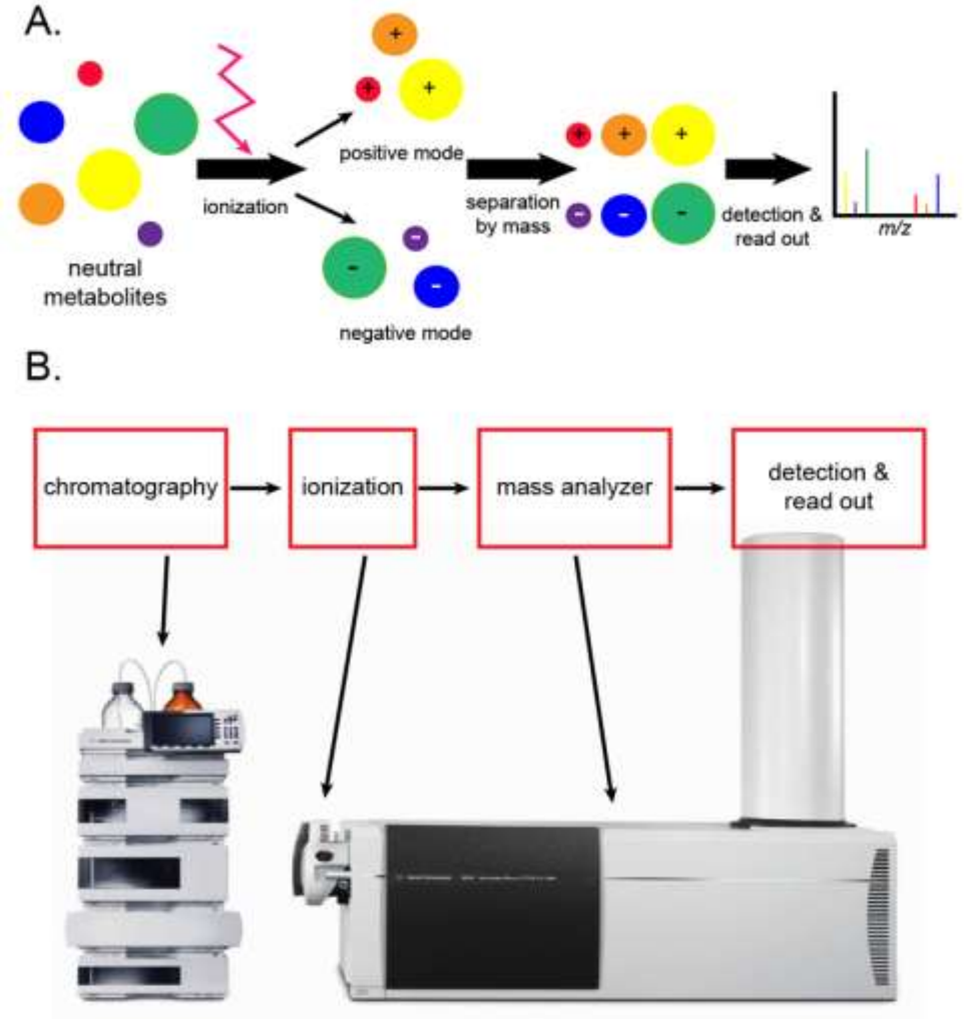


Fig 3-Liquid Chromatography-Mass Spectrometry (LC/MS

Antibiotic residues in milk pose a serious risk to consumer health and pose a financial burden to the dairy industry. This study uses liquid chromatography in conjunction with tandem mass spectrometry (LC-MS/MS) and a fast screening test (BetaStar ® Combo) to compare the presence of antibiotic residues in raw milk. Three dairy firms in north-central Algeria (Algiers and Blida) provided a total of 445 samples for collection. and they underwent quick screening for tetracyclines and β-lactams; 52 samples, including 34 positive tankertruck milk samples and 18 negative bulk-tank milk samples, were analysed by LC-MS/MS. The results showed that 55.3% of the samples exceeded the Maximum Residue Limit (MRL) and 90.4% of the samples were contaminated (n = 47). The chemicals that were most commonly found were the β-lactams and their metabolites, with the highest values found in cloxacillin (1231 µg/kg) and penicillin G (2062 µg/kg).

False-positive results under field conditions appear to be associated with milk samples showing excessive acidity values (19D) or changes in fat-level (2.7 g/100 mL and 5.6–6.2 g/100 mL), especially for tetracyclines. The fast test yielded a relatively low prevalence (7.64%) of residues; however, LC-MS/MS analysis of flumequine (52 µg/kg), cefaclor (maximum 220 µg/kg), and β-lactam metabolites at Consideration of the management of their toxicological effects on humans and the environment should follow high levels.

LITERATURE REVIEW

Mohammad M. Al. Sanea et.al, 2023, In this review article, the first collection of drugs analyzed through high-performance liquid chromatography coupled with a refractive index detector (HPLC-RI) was discussed. The list of all analyzed drugs was shown, and chromatographic conditions for each method were enumerated, demonstrating a helpful guide for all analysts in quality control units.

Zhao Zhou Li et.al, 2023, With the increasingly serious problem of aminoglycoside antibiotic residues, it is imperative to develop rapid, sensitive and efficient detection methods. This article reviews the detection methods of aminoglycoside antibiotics in animal-derived foods, including enzyme-linked immunosorbent assay, fluorescent immunoassay, chemical immunoassay, affinity sensing assay, lateral flow immunochromatography and molecular imprinted immunoassay.

Devi Astri Rahmawati et.al, 2023, The purpose of this article to review the validation and content of antibiotics using various chromatographic and spectrophotometric methods. This review article used five analytical methods on antibiotics, namely high-performance liquid chromatography (HPLC), Fourier transform infrared (FTIR), gas chromatography (GC), ultraviolet-visible (UV-Vis) spectrophotometer and liquid chromatography/mass spectrophotometer (LC/MS) methods. Antibiotics are the most widely used drugs for infections caused by bacteria.

J. Peris Vicente et.al, 2022, This review is the result of a survey across the bibliography about the determination of several antibiotics in biological, food and environmental samples by liquid chromatography. Their determination in those samples is usually made in clinical monitoring, food safety and environmental studies. A brief description of the pharmacological activity is provided, to complement the relevance of the topic bioanalytical method.

Ileana Romana Barac et.al, 2022, Infectious keratitis is a severe infection of the eye, which requires urgent care in order to prevent permanent complications. Typical cases are usually diagnosed clinically, whereas severe cases also require additional tools, such as direct microscopy, corneal cultures, molecular techniques, or ophthalmic imaging. The initial treatment is empirical, based on the suspected etiology, and is later adjusted as needed. It ranges from topical administration of active substances to oral drugs, or to complex surgeries in advanced situations.

Brij Mohan et.al, 2022, Mercury is considered as a highly toxic metal ion due to its lethal effects on humans and the ecological system. The increasing level of antimicrobial resistance are threatening to the ecosystem, public health and economy. The development of new environmentally safe organic molecules can be a potential cure for both of the above-mentioned problems. Herein, we have synthesized 2,7-diamino-3-phenylazo-6-phenylpyrazolo[1,5-a]pyrimidine (PPD) as a new hetero-cyclic ligand, act as a selective Hg^{2+} ion chemosensor.

A Bakar Knu et.al, 2021, This review article compares and contrasts sample preparation techniques coupled with high-performance liquid chromatography (HPLC) and describes applications developed in biomedical, forensics, and environmental/industrial hygiene in the last two decades. The proper sample preparation technique can offer valued data for a targeted application when coupled to HPLC and a suitable detector. Improvements in sample preparation techniques in the last two decades have resulted in efficient extraction, cleanup, and preconcentration in a single step, thus providing a pathway to tackle complex matrix applications.

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V. Selvaraj et.al, 2021, The continuous growth of population and increasing industrial activities in the different sectors, viz., textiles, leather, plastics, cosmetics and food processing industries require the development of varying nature of novel dyes. Among the dyes used in different industries, azo dyes are considered to be the most widely consumed and play an important role in the dyeing of textiles, leather, and plastics, etc. Azo dyes and their degradation products are toxic toward aquatic life and mutagenic for humans. The textile industry is one of the major contributors of azo dye pollutants and discharges the large quantity of azo dye effluents, which causes an acute hazardous effect on environment and human health.

Henein et.al, 2020, Infectious keratitis is a major cause for corneal blindness globally. Broad-spectrum antimicrobial therapy is currently the standard treatment, but there is a growing need for alternative or adjuvant antimicrobial treatment, due to the emerging antimicrobial resistance, long treatment duration and cost of treatment. Photoactivated chromophore for keratitis - corneal collagen cross-linking has been increasingly used as an adjuvant treatment for infectious keratitis but high-quality evidence is limited.

Erwin Adams et.al, 2020, Amikacin, gentamicin and tobramycin are aminoglycoside antibiotics mostly used for the treatment of a wide range of aerobic Gram negative bacteria. Lack of a UV chromophore as well as their polar and non-volatile nature make direct determination of these aminoglycosides by conventional LC and GC very challenging. Existing analytical methodology is either expensive, complicated or time consuming. In this work, a thin layer chromatography – flame ionization method was developed for fast analysis of these aminoglycosides in pharmaceutical formulations. Paromomycin was used as internal standard for quantitation. Development of the rod with one single solvent mixture was sufficient to achieve the desired separation of target components. Good determination coefficients (>0.997) were achieved for all target analytes.

RATIONALE OF STUDY

Increasing Antibiotic Resistance:

Addressing the global challenge of antibiotic resistance necessitates advanced analytical methods for precise antibiotic analysis.

Complexity of Antibiotic Mixtures:

Many pharmaceutical formulations and environmental samples contain complex mixtures of antibiotics, requiring a sophisticated analytical approach.

Need for Selective Detection:

Traditional methods may lack the specificity needed to differentiate between various antibiotics, highlighting the need for a selective chromophoric method.

Advancements in Analytical Chemistry:

Leveraging recent advancements in analytical chemistry, the development of a chromophoric method aligns with current technological capabilities.

Environmental Monitoring:

With antibiotics entering ecosystems through various routes, an effective analytical method becomes crucial for monitoring and mitigating environmental impacts.

Pharmaceutical Quality Control:

Pharmaceutical industries require robust methods for quality control of antibiotic formulations, emphasizing the importance of an advanced analytical technique.

Plan of work

1. **Selection of Antibiotic and Chromosphere**
2. **Development of Analytical Method**
3. **Calibration Curve**
4. **Validation and Method Performance**
5. **Method Comparison and Validation**
6. **Documentation and Reporting**

Aim

To critically review the development of chromophoric matrices for the analysis of antibiotics, examining methodologies, advancements, and applications in order to assess the current state of the field and identify potential areas for improvement and future research.

Objectives

Evaluate Existing Chromophoric Matrices:

Examine and assess the current state of chromophoric matrices used in antibiotic analysis, considering their methodologies, strengths, and limitations.

Identify Antibiotic Classes Addressed:

Categorize and analyze the effectiveness of chromophoric matrices in addressing various classes of antibiotics, emphasizing the specificity and sensitivity achieved.

Explore Chemical Interactions:

Investigate the chemical interactions between selected chromophores and antibiotics, emphasizing how these interactions contribute to the analytical capabilities of the matrix.

Assess Sensitivity and Quantification:

Critically evaluate the sensitivity of existing matrices in detecting trace amounts of antibiotics and assess the quantification accuracy achieved under different experimental conditions.

CONCLUSION

Antibiotic quantitative analysis was conducted utilizing a variety of methods that have been discussed in detail above. HPLC was selected out of all the procedures described since it is effective and selective. Antibiotics can be quantitatively analyzed using HPLC without the need for extraction antibiotics. Because the infusion component lacks a chromophore group, this is possible. Thus, the Spectrophotometer will not pick up infusion as a detector. Because most antibiotics have easily detectable chromophores (aromatic molecules, carbonyl, carboxylate, and amido), the Spectrophotometer can be employed as a detector.

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