pH AND SODIUM BENZOATE EVALUATION IN SOME COUGH SYRUPS OBTAINED IN BENIN CITY

EMMANUEL DANIEL OVUWONYE

MAT NO: PSCI908783

A PROJECT WORK SUBMITTED TO THE DEPARTMENT OF CHEMISTRY, FACULTY OF PHYSICAL SCIENCES, UNIVERSITY OF BENIN, BENIN CITY, EDO STATE, NIGERIA. IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF BACHELOR OF SCIENCE DEGREE IN INDUSTRIAL CHEMISTRY.

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DECLARATION

I hereby declare that this project has been undertaken by **EMMANUEL DANIEL OVUWONYE**, with the Matriculation Number **PSC1908783**, a student of Department Of Chemistry, Faculty Of Physical Sciences, University Of Benin. In partial fulfillment of the award of Bachelor of Science (B.Sc.) degree in industrial chemistry.

____________________________ __________________

Emmanuel Daniel Ovuwonye **Date**

CERTIFICATION

This is to certify that this project work was carried out by **EMMANUEL DANIEL OVUWONYE** with the Matriculation Number **PSC1908783** a student of Department of Chemistry, Faculty of Physical Sciences, University of Benin, Benin City under the supervision of **Dr. E.N. Dibie** in partial fulfillment of the requirement for the award of Bachelor of Science (B.Sc.) Honour in Industrial Chemistry.

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Prof. J.U. Iyasele **Date**

(Head of Department)

DEDICATION

This research work is dedicated first and foremost to God Almighty, who has been my backbone and pillar of support and has helped me scale through from the beginning to the successful climax, to the Department Of Chemistry, University of Benin, that have equipped me so far with the necessary theoretical and practical knowledge to carry out any research work pertained to Chemistry and beyond, to my amazing Supervisor, Dr. E.N. Dibie, who has been more receptive and considerate all through this research work and to my Parents who has been there for me financially.

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ABSTRACT

In this work, pH and sodium benzoate constituents of some brands of cough syrup preparations marketed in Benin City were investigated. The cough syrups (three different brands) were obtained from pharmaceutical stores in Benin City and standard methods were used for the various determinations. Findings indicated that the studied cough syrups' pH ranged from 4.11 to 5.61.Sodium benzoate values ranged between 214.90ppm and 217.25ppm. Variations in the values of the parameters analyzed clearly suggested the need for emphases on good manufacturing and storage practices among drugs handlings

CHAPTER ONE

INTRODUCTION AND LITERATURE REVIEW

1.1. INTRODUCTION

Cough is a defensive reaction that forcefully expels air from the lungs to eliminate irritants and mucus from your airways (Mayo Foundation for Medical Education and Research, 2023). Triggers can include inhaled particles like dust or smoke, postnasal drip from allergies or colds, and underlying medical disorders such as asthma (National Heart, Lung, and Blood Institute, 2023). The cough reflex involves irritation in the airways transmitting signals to the brain's cough center, which subsequently orders muscles to contract and forcibly expel air, ideally dislodging and eliminating the irritant (Baughman, 2016). Coughs can be productive (wet), bringing up mucus to remove congestion, or non-productive (dry), affording no relief and typically triggered by irritation. Treatment depends on the cause, with options ranging from over-the-counter drugs like expectorants and cough suppressants or medications to address symptoms or the underlying cause such as infection with antibiotics. If the cough is severe, persistent, or accompanied by other troubling symptoms like fever, shortness of breath, or blood in the mucus, consult a healthcare expert for correct diagnosis and treatment (Mayo Foundation for Medical Education and Research, 2023).

Cough syrup, in various forms, has been used for millennia to ease cough symptoms and throat irritation. The history of cough syrup can be traced back to ancient civilizations where natural treatments were applied to relieve respiratory problems (Vidyasagar *et al.,* 2010). These syrups often contain active substances that target distinct parts of the cough response. For example, some may contain expectorants i.e guaifenesin which help release mucus, while others may contain cough suppressants i.e dextromethorphan that directly impact the cough center in the brain. However, cough syrups often integrate extra substances beyond the active components such additional compounds include: preservatives, sweeteners, flavouring agents, colouring agents, etc.

Regulatory requirements were developed to ensure the quality and safety of cough syrups, while modern trends have seen an increasing demand for natural and herbal medicines, spurring the development of cough syrups including botanical substances. Today, cough syrup remains a popular over-the-counter medication, giving a choice of solutions to address different types of coughs and respiratory ailments.

Cough syrups are a fixture in many households, offering relief from coughs and congestion for individuals of all ages. However, assuring their safety and efficacy relies greatly on their composition and the presence of diverse chemicals. Among these additives, sodium benzoate plays essential roles. Sodium benzoate functions as a preservative, prolonging the shelf life of the syrup and reducing microbiological growth. The pH level of cough syrup is crucial for assessing the effectiveness of its preservation characteristics, which are vital for guaranteeing product stability and safety during storage. Cough syrups are often designed to attain a pH that prevents microbial development and ensures stability during their shelf life. Deviations from the ideal pH range, either towards acidity or alkalinity, might affect the performance of preservatives such benzoic acid and sodium benzoate.

While these ingredients perform crucial roles in cough syrups, their excessive intake can cause possible health issues, particularly for vulnerable groups like children (World Health Organization, 2023). Therefore, correct evaluation of their content in cough syrup is vital to assure product quality, efficacy, and compliance with regulatory criteria. Spectrophotometric approaches, notably UV-VIS offers a reliable and frequently adopted strategy for the quantitative study of medicinal or pharmace utical substances (Basavaiah *et al.,* 2007).

1.1.1 BACKGROUND OF STUDY

Sodium benzoate is often employed as preservatives in pharmaceutical formulations such as cough syrups. The measurement of its concentration in these formulations is vital to ensure compliance with regulatory criteria and to assure the safety and efficacy of the product. Sodium benzoate is a frequently utilized preservative due to its capacity to suppress the growth of bacteria, hence extending the shelf life of medicinal items (García-Moreno *et al.,* 2003). However, high intake of sodium benzoate has been related with detrimental health effects, including allergic responses and hyperactivity in children (Tsai *et al.,* 2018). Therefore, correct quantification of sodium benzoate in cough syrups is vital to prevent any health hazards. The pH level of cough syrup considerably determines the efficiency of its preservation characteristics. Preservatives, such as benzoic acid and sodium benzoate, are routinely added to cough syrups to suppress microbial growth. However, the efficacy of these preservatives is pH-dependent, with acidic environments favoring their antibacterial activity. When the pH deviates from the ideal range, either becoming too acidic or too alkaline, the efficiency of the preservatives diminishes, potentially leading to microbial proliferation and product degradation. Understanding the relationship between pH and preservative qualities is vital for optimizing cough syrup compositions and guaranteeing product stability. By maintaining the pH within the required range, manufacturers can maximize the efficacy of preservatives and extend the shelf life of cough syrups, thereby ensuring consumer health.

UV-Vis spectrometry is a commonly utilized analytical technique for the measurement of organic components in pharmaceutical formulations (Mendez *et al.,* 2019). The premise of UV-Vis spectrometry relies on the measurement of absorbance at specific wavelengths, which correlates with the concentration of the analytes in solution. By building standard calibration curves utilizing known amounts of sodium benzoate, its content in a specific cough syrup samples can be properly established.

Several methods have been documented in the literature for the determination of sodium benzoate in pharmaceutical formulations. These approaches include high-performance liquid chromatography (HPLC), capillary electrophoresis (CE), and UV-Vis spectrophotometry (Al-Momani *et al.,* 2019). Among these techniques, UV-Vis spectrophotometry offers advantages such as simplicity, speed, and cost-effectiveness, making it suited for routine quality control examination in pharmaceutical laboratories.

1.1.2 STATEMENT OF PROBLEM

The spectrometric assessment of sodium benzoate content in cough syrup is vital to verify compliance with regulatory standards and determine the efficacy of the preservation qualities of sodium benzoate. Sodium benzoate is widely used in cough syrup formulations to limit microbial development and ensure product stability. Regulatory agencies set maximum allowable limits for sodium benzoate concentration in cough syrup formulations to ensure consumer safety and product quality (The Food and Drug Administration [FDA] allows up to a 0.1% concentration of sodium benzoate by weight in foods and beverages which is also applicable to pharmaceutical product like cough syrup). However, fluctuations in sodium benzoate concentration may occur during manufacturing, storage, or handling, potentially resulting to non-compliance with regulatory standards.

Moreover, the effect of pH on the preservation characteristics of sodium benzoate in cough syrup is a serious problem. pH levels within cough syrup formulations can influence the antibacterial activity of sodium benzoate, with acidic circumstances generally improving its efficiency. Understanding how pH changes affect the preservative characteristics of sodium benzoate is crucial for optimizing cough syrup compositions and providing adequate microbiological protection.

Therefore, this study attempts to address two key objectives: first, assessment of sodium benzoate concentration in cough syrup, assuring compliance with regulatory norms. Second, to explore the influence of pH on the preservation qualities of sodium benzoate in cough syrup compositions, revealing its impact on microbial suppression and product stability.

1.1.3 JUSTIFICATION OF STUDY

Measuring the amount of sodium benzoate in cough syrup using spectrophotometric method and investigating how pH influences its ability to preserve the syrup is vital for manufacturing safe cough syrup. Regulations set limitations on sodium benzoate to keep consumers safe. But how well sodium benzoate works depends on the syrup's pH and other factors. By addressing this critical requirement, the proposed study intends to contribute to pharmaceutical science and ensure the quality and safety of cough syrup products. Spectrophotometric technique is a precise way to detect sodium benzoate levels, which is vital for obeying laws and manufacturing better syrup.

1.1.4 SCOPE OF WORK

Three different cough syrups (Exiplon Expectorant, Menthodex Cough Mixture, Coflin Cough Linctus) were purchased from some pharmacy store in Benin, Edo state. The concentration of sodium benzoate in the different cough syrup brand were determined using T80 Uv/Vis spectrometer at the department of pharmarcy, University of Benin, the pH of the various sample were analyzed with a digital pH meter. The data obtained is then compared.

1.1.5 AIM AND OBJECTIVES

AIM: The aim of this work is to determine the concentration of sodium benzoate in three different cough syrup formulation, ensuring compliance with regulatory standards as well as the determination of the pH of the cough syrups to see possible relationships.

OBJECTIVES: The objectives of this study are to:

1. Determine the concentration of sodium benzoate in the various cough syrup samples.
2. Determine the pH of the various cough syrup samples.
3. Evaluate possible relationship between the concentration of sodium benzoate in the cough syrup samples and the pH of the samples.

1.2. LITERATURE REVIEW

1.2.1. BRIEF HISTORY OF COUGH AND COUGH SYRUP

The act of coughing, a response aimed at cleaning the throat and airways of irritants, has been a human experience since antiquity. Throughout history, different civilizations, including the Egyptians, Greeks, and Romans, chronicled cures for cough symptoms in their medical literature. These early remedies frequently depended on natural components like herbs, honey, and wine, reflecting empirical observations rather than a thorough grasp of cough's mechanics (Porter, 2008).

By the late 19th and early 20th centuries, non-opioid antitussives such ammonium chloride and chloroform found their way into cough syrup compositions (Porter, 2008). The mid-20th century represented a substantial move away from opioid-based therapy, spurred by increased regulatory scrutiny and the discovery of safer alternatives. Subsequent decades witnessed the development of cough syrup compositions, integrating a varied array of active substances with varying modes of action. Antitussives such as dextromethorphan gained importance, alongside expectorants like guaifenesin and decongestants like pseudoephedrine (Porter, 2008). These breakthroughs were underpinned by continuous scientific inquiry into cough pathogenesis and treatment innovation. In current times, the emphasis on evidence-based medicine has spurred attempts to enhance cough syrup compositions for efficacy, safety, and patient adherence. Pharmaceutical research continues to investigate innovative therapeutic routes and modify existing medications to better address the varied character of cough symptoms (Dicpinigaitis and Morice, 2021). Despite developing medical procedures, cough syrup remains a popular over-the-counter treatment for reducing cough linked with varied respiratory disorders. However, current conversations and research attempts underline the need of understanding cough's intricacies and personalizing therapies to individual needs.

1.2.2. DESCRIPTION OF COUGH SYRUP

Cough syrups are a prominent over-the-counter drug intended to treat symptoms linked with coughs (Mayo Foundation for Medical Education and Research, 2023). Available in various formulas and tastes for both adults and children, these syrups target distinct components of the cough response to provide relief. It often comprises of a mixture of active substances such as antitussives (to suppress cough), expectorants (to thin and loosen mucus), decongestants (to relieve nasal congestion), and sometimes analgesics (to ease pain) (British Pharmacopoeia Commission, 2019). These active components are generally dissolved or contained in a sweetened syrup basis for convenience of administration, typically orally (Reynolds, 2009). Cough syrup compositions vary widely based on the specific symptoms they are supposed to address. For instance, cough syrups advertised for dry, non-productive coughs commonly contain antitussives such as dextromethorphan or codeine, which work on the cough center in the brain to inhibit the impulse to cough (Sweetman, 2018). Conversely, products intended with productive coughs may contain expectorants like guaifenesin, which function by raising the volume and lowering the viscosity of respiratory tract secretions, making them easier to expel (World Health Organization, 2007).

In addition to these active chemicals, cough syrups may also contain various additives such as flavorings, sweeteners, and colorants to increase palatability and appearance. Some formulations may also include alcohol as a solvent or preservative, however alcohol-free versions are also available for persons who need to avoid alcohol use (British Pharmacopoeia Commission, 2019).

Cough syrups address coughs through various mechanisms:

- **Expectorants:** Expectorants are a family of medications frequently found in cough syrups that are intended to help remove mucus and phlegm from the respiratory tract. They function by increasing the production of respiratory tract secretions and lowering their viscosity, making it simpler for the body to remove them by coughing. Expectorants typically function by boosting the activity of the glands in the respiratory tract, leading to the generation of thinner mucus that can be more easily coughed up. One of the most often utilized expectorants in cough syrups is guaifenesin. Guaifenesin acts by increasing the volume and lowering the viscosity of respiratory tract secretions, so allowing their evacuation from the airways. It is typically used in the treatment of productive coughs, where there is an excess buildup of mucus in the respiratory tract.
- **Demulcents:** Demulcents are compounds typically found in cough syrups that function by producing a protective film over inflamed mucous membranes in the throat and respiratory system, offering relief from cough and sore throat symptoms. These compounds are often viscous and stick to the mucosal surfaces, easing discomfort and lowering the urge to cough. Demulcents are typically used in cough syrup formulations alongside other active chemicals such as antitussives, expectorants, and decongestants to provide comprehensive relief from cough symptoms. One of the key mechanisms of action of demulcents is their ability to improve the hydration of mucous membranes, which helps to alleviate dryness and irritation. By establishing a protective covering over the inflamed tissues, demulcents also aid to reduce friction and inflammation, further adding to symptom relief. Additionally, the relaxing effects of demulcents can assist to lower cough reflex sensitivity, resulting to a decrease in the frequency and severity of

coughing episodes. Common demulcents used in cough syrup formulas include natural components such as honey, glycerin, and marshmallow root extract, as well as synthetic chemicals like carboxymethylcellulose and polyethylene glycol. These chemicals are chosen for their capacity to adequately cover and soothe irritated mucous membranes without generating undesirable effects or interactions with other components of the cough syrup. It is crucial to note that while demulcents can provide temporary relief from cough and sore throat symptoms, they do not address the underlying cause of the cough. Therefore, cough syrups containing demulcents are typically used as supplementary therapy alongside other medications or treatments focused at addressing the underlying respiratory problem.

- **Cough Suppressants:** One of the most extensively used cough suppressants is dextromethorphan (DM), which is structurally close to opioids but lacks their analgesic and addictive qualities. Dextromethorphan operates as a non-narcotic antitussive by targeting sigma opioid receptors and decreasing the transmission of cough signals in the central nervous system (Reynolds, 2009).

  Another cough suppressant widely utilised in cough syrup formulations is codeine, a moderate narcotic analgesic with antitussive effects. Codeine operates on the central nervous system by binding to opioid receptors, thereby lowering the sensitivity of the cough reflex and suppressing coughing (British Pharmacopoeia Commission, 2019). While cough suppressants can provide relief from persistent or annoying coughing, it's vital to use them wisely and according to established dose guidelines. Overuse or misuse of cough suppressants, particularly those containing opioids like codeine, can lead to adverse effects such as sleepiness, constipation, and respiratory depression.

Additionally, cough suppressants may not be acceptable for all persons, especially those with certain underlying medical disorders or who are taking other drugs (World Health Organization, 2007).

1.2.3. COUGH SYRUP ADDITIVES

Additives are substances or mixtures of substances added to food or pharmaceuticals and are used in production, processing, storage, packaging of food but are not major ingredients. Beyond the active pharmaceutical ingredients (APIs) that directly target the cough reflex, cough syrups contain a range of additives that contribute to their functionality, palatability, and shelf life. Additives added to cough syrup include:

1. **Excipients:** excipients are a large group of inert substances that are essential to the formulation and administration of cough syrups (The United States Pharmacopeia Convention, 2024). Depending on what they do, they can be divided into more categories:
    - **Sweeteners:** Particularly for paediatric formulations, sugars like sucrose or sugar substitutes like sorbitol improve palatability (The United States Pharmacopoeia Convention, 2024).
    - **Flavourings:** Natural or artificial flavours can cover up the bad taste of some APIs. For instance, cough syrups are frequently flavoured with cherry or grape to make them more kid-friendly (Baughman and Loudon, 2016).
    - **Colorings:** Food-grade colouring compounds improve appearance. To satisfy consumers' need for items that appear more natural, some producers are, nevertheless, choosing to use transparent syrups (The United States Pharmacopoeia Convention, 2024).

- **Solvents:** The most popular solvent for cough syrups is water. Depending on the formulation and intended qualities, alcohol or glycerin may occasionally be added in addition to water (Block, 2011).

2. **Preservatives:** The growth of microorganisms in cough syrups might shorten their shelf life and can be dangerous. Important additions that aid in preventing this include preservatives (National Academies of Sciences, Engineering, and Medicine, 2018). Sodium benzoate is a commonly used preservative in cough syrups. It works by rupturing microorganisms' cell membranes, which prevents them from growing (Block, 2011).
3. **Viscosity Modifiers:** For the best possible distribution and precise dosage, cough syrups must have a specific consistency. Viscosity modifiers, like xanthan gum or acacia, aid in achieving the appropriate thickness and keep the constituents from separating.
4. **Antifoaming Agents:** Shaking or storing certain cough syrups may cause them to foam. Simethicone is one example of an antifoaming ingredient that helps keep excessive foaming in check and guarantee a more uniform outcome.
5. **Buffers:** The stability and effectiveness of several cough syrups depend on maintaining a particular pH range. In syrup, buffers aid in pH regulation and stop undesirable chemical reactions (Block, 2011).
6. **Alcohol:** Although it's not always present, a tiny quantity of alcohol (usually less than 10%) is present in some cough syrups as a solvent, preservative, or to improve the effectiveness of specific APIs (Baughman and Loudon, 2016). It's vital to remember that children or people with specific medical conditions shouldn't use cough syrups that contain alcohol.

1.2.4. REPORTED USES OF COUGH SYRUP

Abuse for recreational purposes: Cough syrup has been used for recreational purposes, especially by teenagers and young adults who are looking for euphoria or altered states of consciousness. Cough syrups with chemicals like dextromethorphan or codeine are frequently used in excess, which can have harmful side effects and result in intoxication (Babu and Brent, 2014).

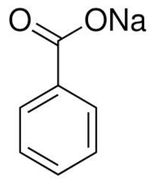
Cough Symptom Relief: Cough syrup is primarily used to treat the symptoms of cough that are brought on by a variety of respiratory illnesses, including allergies, bronchitis, the common cold, and the flu. Antitussives, expectorants, or combination compounds used in cough syrup formulas inhibit coughing, lessen mucus production, or loosen phlegm, offering momentary respite from cough symptoms (Lexicomp, 2022).

Treatment for Paediatric Cough: In paediatric medicine, cough syrup is often used to treat children's cough symptoms. To reduce the possibility of negative effects, especially in young children, healthcare professionals must be cautious and follow age-appropriate dosage recommendations (Unguru *et al.,* 2016).

Management of Chronic Cough: Cough syrup may be used as a part of a therapy plan for those whose cough lasts longer than eight weeks. A multidisciplinary strategy, involving lifestyle changes, medication, and treating underlying medical issues, may be necessary to manage chronic cough, which can be difficult to treat (Morice *et al.,* 2020).

Preoperative Cough Suppression: Cough syrup may occasionally be given before to surgery under general anaesthesia in order to control cough reflexes. This reduces the possibility of issues like aspiration during anaesthesia induction and airway care (Lexicomp, 2022).

1.2.5. GENERAL DESCRIPTION OF SODIUM BENZOATE



Sodium benzoate

(C7H5NaO2)

Sodium benzoate is a common preservative that finds use in a variety of sectors, such as medicine, pharmaceutical and food. It is the sodium salt of benzoic acid, a naturally occurring chemical component that can be found in cinnamon and some fruits (plums, berries) (National Institutes of Health, 2023). It is a crystalline, white powder that dissolves easily in water. When used at permissible amounts established by regulatory agencies such as the FDA (U.S. Food and Drug Administration), it is widely regarded as safe (National Academies of Sciences, Engineering, and Medicine, 2018). Nonetheless, there have been a few documented instances of uncommon allergic responses to sodium benzoate (Mayo Clinic, 2023).

The reason sodium benzoate works so well as a preservative is because it can stop microbiological growth. It operates through:

Intracellular Acidification: Bacteria and fungi's cells are permeable to sodium benzoate. Once inside, it increases acidity, upsetting their internal pH equilibrium. This acidic environment prevents vital cellular functions and eventually results in microbial death (Block, 2011). **Activity in Undissociated Form:** Benzoic acid, the undissociated form of sodium benzoate, is principally responsible for its antibacterial effect. This form is more likely to break through the microbial cell membrane and cause havoc there (Russell and Chopra, 2005).

1.2.6. ROLES OF SODIUM BENZOATE IN COUGH SYRUP

Preservation: Sodium benzoate is used as a preservative in cough syrup formulations, which helps to keep the drug free of microorganisms and prolong its shelf life (Ghosh, 2017).

Microbial Stability: Sodium benzoate helps keep cough syrup microbially stable by preventing the growth of bacteria, yeast, and mould. This lowers the danger of spoiling and guarantees product safety (Patel *et al.,* 2020).

pH-Dependent Efficacy: Sodium benzoate's antibacterial activity is pH-dependent, working best in acidic settings. To improve the effectiveness of the preservative, cough syrup formulations frequently have their pH changed to an acidic state (Jayabalan *et al.,* 2014).

Regulatory Approval: The US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have approved the use of sodium benzoate as a preservative in pharmaceutical products, including cough syrups (Food and Drug Administration, 2021).

1.2.7. GENERAL DESCRIPTION OF pH

pH is a quantitative measure of the acidity or alkalinity of a solution, often known as the potential of hydrogen. The concentration of hydrogen ions (H^+) in the solution determines it. The pH scale spans from 0 to 14, where a pH of 7 is regarded as neutral. those with a pH value below 7 are considered acidic, whereas those with a pH value over 7 are considered alkaline or basic. When acids are dissolved in water, they release hydrogen ions, which leads to an increase in the concentration of H^+ ions and a decrease in the pH of the solution. Conversely, bases have the ability to either take hydrogen ions or release hydroxide ions (OH^-), resulting in a decrease in the concentration of H^+ ions and an increase in the pH of the solution.

The acidity or alkalinity of a solution, as measured by its pH, can exert substantial influence on chemical reactions, biological activities, and the characteristics of substances that are dissolved in the solution. Several biological systems, such as blood, saliva, and cellular environs, regulate their pH within a specific range to ensure optimal functioning.

Ph As A Stabilizer In cough syrup

Chemical reactions are influenced by pH. Maintaining a specific pH range can promote stability in cough syrups by:

- **Optimizing Active Ingredient Functionality:** Certain cough syrups contain active pharmaceutical ingredients (APIs) that perform better within a particular pH range. For instance, some cough suppressants could breakdown more rapidly in very alkaline settings (Aulton and Taylor, 2013).
- **Minimizing Chemical Degradation:** Cough syrups can contain diverse components like sweets, flavors, and preservatives. An appropriate pH can assist in avoiding undesirable chemical reactions between these constituents, guaranteeing the syrup's integrity over its shelf life (Block, 2011).
- **Preservative Efficacy:** Some preservatives often used in cough syrups, like sodium benzoate, perform more successfully in acidic environments (about pH 5.5) (Block, 2011). Maintaining a slightly acidic pH can boost the preservative's capacity to suppress microbial development and extend the syrup's shelf life.

Ph Range In Cough Syrup

The pH of cough syrups might vary based on the precise composition and chemicals utilized. However, cough syrups often lie within a slightly acidic to neutral pH range (about pH 5.0 to pH 7.0) (Baughman and Loudon, 2016). This collection offers a balance between the stability of active substances, palatability, and preservative effectiveness.

1.2.8. pH TECHNIQUES AND PRINCIPLES

The idea of pH, or potential of hydrogen, is a fundamental principle in chemistry and biology that assesses the acidity or alkalinity of a solution. It is defined as the negative logarithm of the concentration of hydrogen ions (H^+) in a solution. The pH scale spans from 0 to 14, with a pH of 7 considered neutral. Solutions with a pH less than 7 are acidic, whereas those with a pH more than 7 are alkaline or basic. Several ways are widely applied to determine pH accurately:

pH Meter: A pH meter is a precision tool used to measure the pH of a solution. It comprises of a glass electrode and a reference electrode immersed in the solution, coupled to a voltmeter. The glass electrode responds to variations in hydrogen ion concentration, giving a voltage signal proportional to the pH of the solution. pH meters are frequently utilized in laboratories, factories, and research settings due to their precision and reliability (Grubisha *et al.,* 2014).

pH Indicator Papers: pH indicator papers are basic, affordable tools used to measure the pH of a solution qualitatively example include litmus paper. These sheets feature chemical indicators that change color in response to differences in pH. By comparing the color of the indicator paper to a color chart provided by the manufacturer, users can approximate the pH of the solution within a certain range (Başkan and Gürkan, 2018).

pH Titration: pH titration includes the steady addition of a titrant solution of known pH to the solution being analyzed until the pH reaches a desired endpoint. This technique is often used to assess the acidity or alkalinity of solutions, find the equivalence point of acid-base processes, and quantify the quantity of acids or bases in a sample (Hassan, 2017).

These pH approaches, along with others such as pH electrodes and pH probes, serve vital roles in different scientific fields, including chemistry, biology, environmental science, and medicine, permitting the accurate measurement and regulation of pH in diverse applications.

1.2.9. TECHNIQUES AND PRINCIPLES OF SPECTROPHOMETRY

Spectrophotometry is a strong analytical technique used to quantify the absorbance or transmission of light by a substance as a function of wavelength. It depends on the idea that different substances absorb light at specific wavelengths, allowing for qualitative and quantitative study of numerous molecules in solution.

The fundamental components of a spectrophotometer comprise a light source, a monochromator or wavelength selector, a sample holding or cuvette, and a detector. The light source emits light of a certain wavelength range, which is transmitted through the sample solution in the cuvette. The monochromator chooses a single wavelength of light, and the detector detects the intensity of light either absorbed or transmitted by the sample. The resulting absorbance or transmission spectrum offers information about the concentration, identification, and characteristics of the analyte.

Spectrophotometry can be performed in either the ultraviolet (UV), visible (Vis), or infrared (IR) parts of the electromagnetic spectrum, depending on the type of analysis and the parameters of the sample. UV-Vis spectrophotometry is widely used for qualitative and quantitative investigation of organic and inorganic substances, including nucleic acids, proteins, medicines, and environmental contaminants. IR spectrophotometry, on the other hand, is extensively applied for the structural characterisation of organic compounds based on their unique vibrational modes.

Fundamental Principles of spectrophotometry

Light and Matter: Light, a kind of electromagnetic energy, exists as a spectrum with varied wavelengths. When light interacts with materials, numerous phenomena can occur, including absorption, reflection, and scattering. Spectrophotometry focuses on the absorption of light by a sample.

Absorption and Beer-Lambert Law: Certain molecules or atoms inside a sample can absorb specific wavelengths of light. The Beer-Lambert Law, a fundamental principle in spectrophotometry, quantifies this relationship. It asserts that for a dilute solution the amount of light absorbed (measured as absorbance) is directly proportional to the concentration of the absorbing species in the sample and the path length of the light going through the sample (Skoog *et al.,* 2014). The Beer-Lambert law asserts that there is a linear connection between the concentration and the absorbance of the solution, which enables the concentration of a solution to be estimated by measuring its absorbance.

$$A = \varepsilon c l$$

A	Absorbance	
ε	Molar absorption coefficient	$M^{-1}cm^{-1}$
c	Molar concentration	M
l	optical path length	cm

Techniques In Spectrophotmetry

There are two main types of spectrophotometers based on the light source and measurement:

1. **Absorption Spectrophotometry** :

   An absorption spectrophotometer typically comprises a light source, a monochromator, a sample cuvette, a detection, and a signal processing device. The light source emits a broad spectrum of light, which is subsequently collimated and transmitted via a monochromator. The monochromator chooses a certain wavelength of light and focuses it towards the sample enclosed in a clear cuvette. The detector on the other side of the cuvette detects the intensity of the transmitted light. By comparing the intensity of the incident light with the transmitted light, the amount of light absorbed by the sample may be estimated. Using the Beer-Lambert Law, the concentration of the absorbing species in the sample can be estimated. There are two primary categories of absorption spectrophotometry:

Ultraviolet-Visible (UV-Vis) Spectrophotometry: Analyzes the absorption of light in the ultraviolet (UV) and visible (Vis) sections of the electromagnetic spectrum. This approach is often used to identify and measure diverse chemical compounds based on their unique UV-Vis absorption patterns.

Infrared (IR) Spectrophotometry: Focuses on the absorption of light in the infrared (IR) range. IR spectroscopy offers information on the functional groups present in a molecule due to characteristic vibrational and rotational motions inside the molecule.

2. Emission Spectrophotometry:

In emission spectrophotometry, the sample is initially excited using an external energy source (e.g., light or heat). The excited atoms or molecules in the sample then return to their ground state by producing light at precise wavelengths. This emitted light is measured by the equipment.

Emission spectrophotometry is generally used for elemental analysis, as various elements emit unique wavelengths of light upon stimulation.

This technique is effective in identifying and quantifying the presence of metals and other elements in a sample.

Advantages of Spectrophotometric Method:

Quantitative: Spectrophotometry provides for the measurement of individual analytes in a sample based on the Beer-Lambert Law.

Specificity: Many compounds have unique absorption or emission spectra, enabling specific identification of components within a mixture.

Wide Range of Applications: Spectrophotometry can be employed to assess many samples, including liquids, solids, and gases, making it a flexible analytical technique.

CHAPTER TWO

MATERIALS AND METHODS

2.1 MATERIALS

2.1.1 SOLVENTS AND REAGENTS

1. Sodium benzoate
2. Distilled water
3. Buffer 4.01
4. Buffer 7
5. Buffer 9

2.1.2 APPARATUS

1. Beakers
2. Standard flask
3. Measuring cylinder
4. Sample bottles
5. Stirrer

2.1.3 EQUIPMENTS

1. UV/VIS Spectrophotometer
2. Digital pH meter
3. Analytical balance

2.1.4 OTHERS

1. Hand gloves
2. Cotton wool and tissue papers
3. Whatman filterpapers

2.2 METHOD

2.2.1 SAMPLE COLLECTION

Three different cough syrups (Exiplon Expectorant, Menthodex Cough Mixture, Coflin Cough Linctus) were purchased from some Pharmacy in Benin, Edo state, and stored at project laboratory, University of Benin, at a temperature ranging from 28^{o}C to 34^{o}C.

Table (1): Cough syrups (generic names), Contents and Batch numbers

S/N	Cough syrup names	Content	Batch number
1	Exiplon Expectorant	Diphenydramin hydrocholoride B.P, Sodium citrate B.P, Menthol U.S.P, Ephedrine hydrochloride B.P.	EXE 4031
2	Coflin Cough Linctus	Chloropheniramine maleate B.P, Ammonium chloride B.P, Menthol U.S.P, Ephedrine hydrochloride B.P.	L41023
3	Menthodex Cough Mixture	Ammonium chloride B.P, Sodium citrate B.P, Menthol B.P, Squill tincture B.P.	697J1

2.2.2 PREPARATION OF STANDARD AND LINEARITY SOLUTION

100mg (0.1g) of standard sodium benzoate was dissolved in 100ml (0.1L) volumetric flask by using distilled water to obtain 1000ppm of sodium benzoate stock solution. Dilution of the stock solution were made by distilled water to yield (50, 45, 40, 35, 30, 25, 20, 25, 10, 5) ppm of sodium benzoate standard solution.

Spectrophotometric measurements of sodium benzoate were carried out by means of UV-VIS spectrophotometer (T80 UV/VIS spectrometer), using 1 cm quartz cell. The absorption bands of the aqueous sodium benzoate solutions were recorded over the wavelength 200 – 400 nm.

Preparation of Calibration Curve

The absorbance of each standard solution was measured at absorption maximum of 221 nm using 1cm quartz cuvette. The absorbance values were then plotted against concentrations to generate a standard calibration curve. Table (2) shows the relationship between each concentration of sodium benzoate and its absorption value.

2.2.3 PREPARATION OF SAMPLE

All investigated cough syrup samples were diluted appropriately (1/5) and were analyzed directly without any further preparation steps such as extraction or concentration. Part of each of the test sample was introduced to the spectrophotometric cell and the molecular absorption was measured at the maximum wavelength (221 nm) for sodium benzoate.

2.2.4 pH ANALYSIS

The PH of each cough syrup was determined at room temperature using a digital pH meter placed directly into each cough syrup sample.

Firstly, three buffer solutions were prepared (from the buffer powder) with following pH: 4.01 7.0, 9.0. The meter was thereafter adjusted with 4.01 and 9.0 buffers and made to accurately detect the buffer solution at pH 7.0 before it was used.

Twenty (20) ml of each cough syrup sample was dispensed into three separate beakers (A, B and C) i.e each beaker receive 20 ml syrup sample and the meter dipped into the samples to obtain triplicate digital pH values, this procedure was repeated for all the three samples including the control. Sprite, a known acidic soft drink was used as control because its pH has been previously studied.

CHAPTER THREE

RESULTS AND DISCUSSION

3.1 RESULTS

3.1.1 RELATIONSHIP BETEWEEEN CONCENTRATON AND ABSORPTION

Table (2): Relationship between the concentration and the absorption of sodium benzoate standard solution**.**

Concentration (ppm) of sodium benzoate	**Absorbance at 211nm**
5	0.30
10	0.55
15	0.90
20	1.20
25	1.45
30	1.75
35	2.00
40	2.35
45	2.65
50	2.90

3.1.2 Calibration Graph

Calibration curves drawn by plotting the absorbance against concentration and limit of detections were found out. Linearity of the curves was validated by the value of correlation coefficients (r2 = 0.999) shown in Fig. 1

Fig.1

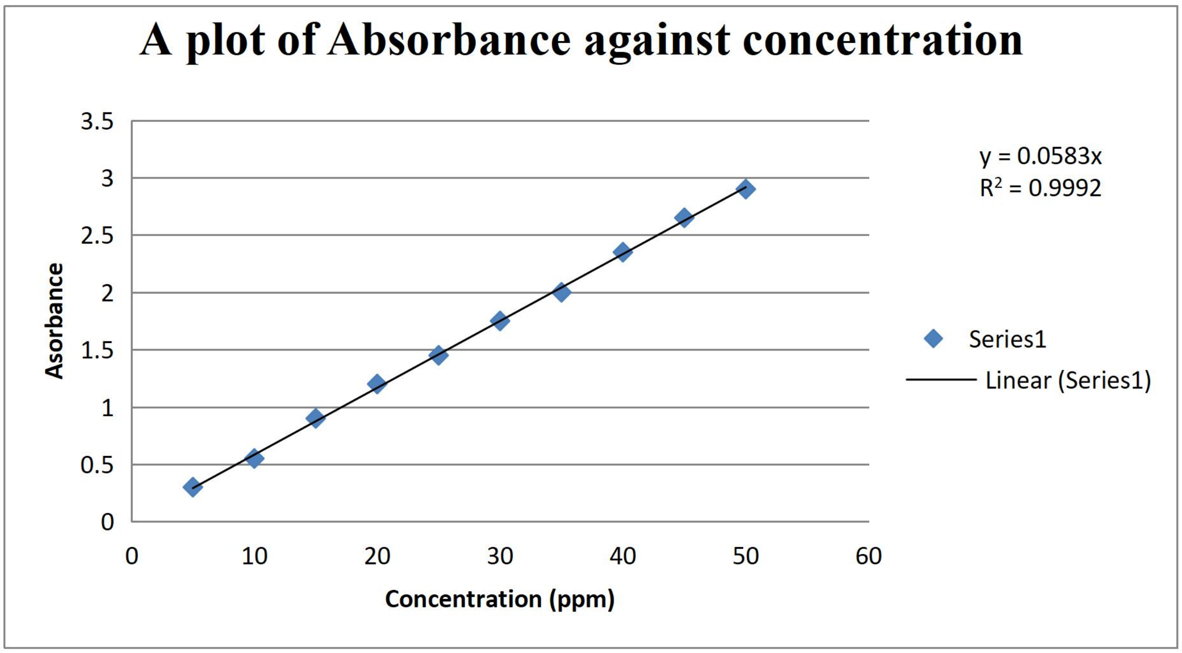


Fig.1 Calibration curve of sodium benzoate

3.1.3 CONTENT LEVEL OF SODIUM BENZOATE IN SAMPLES FROM UV-VIS DATA

The results obtained from this study are presented in Table (3) this, shows the concentrations of sodium benzoate in the three different cough syrup samples.

Table (3):

Cough Syrup	Volume of syrups/100ml	Absorbance at 221nm	Concentration (ppm) of sodium benzoate/20ml	Concentration (ppm) of sodium benzoate in cough syrup
Exiplon Expectorant	20	2.493	42.98	214.90
Coflin Cough Linctus	20	2.521	43.33	216.65
Menthodex Cough Mixture	20	2.553	43.45	217.25

3.1.4 pH DATA FROM pH ANALYSIS

Mean pH values for cough syrup samples

Table (4):

Cough Syrup Names	A	B	C	Mean pH±SD
Sprite (control)	2.99	2.98	2.98	2.98 ± 0.007
Exiplon Expectorant	5.41	5.42	5.40	5.41 ± 0.010
Coflin Cough Linctus	4.10	4.12	4.10	4.11 ± 0.012
Menthodex Cough Mixture	5.61	5.60	5.62	5.61 ± 0.012

3.1.5 CORRELATION

Table (5) below shows the determined content level of sodium benzoate in the three different cough syrup and it compliance with the Food and Drug Administration (FDA) limit.

Table (5):

Cough Syrup Names	Concentration (ppm)	Concentration (%)	FDA Limit (≤ 0.1%)	pH ± SD
Exiplon Expectorant	214.90	0.0215	compliant	5.41±0.010
Coflin Cough Linctus	216.65	0.0217	compliant	4.11±0.012
Menthodex Cough Mixture	217.25	0.0217	compliant	5.61±0.010

3.2 DISCUSSION

From the above results, the analysis of three different cough syrups, focusing on sodium benzoate concentration and pH, indicates that all samples fall within typical regulatory limits set by the Food and Drug Administration (FDA). Sodium benzoate concentrations in the samples—Exiplon Ecpectorant (214.90 ppm), Coflin Cough Linctus (216.65 ppm), and Menthodex Cough Mixture (217.25 ppm)—are significantly below the common limit of 0.1% by weight (1,000 ppm). The pH values—5.41 for Exiplon Expectorant, 4.11 for Coflin Cough Linctus, and 5.61 for Menthodex Cough Mixture—are within the usual range for cough syrups(3.06 – 8.4), suggesting stable formulations. Notably, there's no clear linear relationship between sodium benzoate concentration and pH, indicating that other factors, such as different ingredients or buffer systems, play a larger role in determining pH. Overall, the results suggest these cough syrups are within acceptable regulatory parameters for both sodium benzoate concentration and pH, with the variations in pH likely influenced by other formulation-related components.

3.3 CONCLUSION

This study demonstrates that the sodium benzoate concentrations in these cough syrups are within generally accepted regulatory limits. Additionally, the pH values seem appropriate for cough syrups. The data does not suggest a strong correlation between sodium benzoate concentration and pH, indicating that the variations in pH may be due to other formulation-related factors. Further studies could involve additional cough syrups, a broader examination of formulation components, or deeper analysis of potential interactions to better understand the factors influencing pH and sodium benzoate levels.

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