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Evaluation of Microbiological Contamination of Some Selected Syrups and Suspentions Solid in Katsina Metropolis

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Abstract

Presented study attempted to evaluate the Microbiological contamination of some selected syrups and suspensions sold in Katsina metropolis. This study was conducted in Biological sciences laboratory Al-qalam University Katsina between the months of November 2021 to January 2022. Eighteen different types of oral liquid drugs (9 syrups and 9 suspensions) manufactured in different pharmaceutical industries of Nigeria were microbiologically examined using standard cultural and biochemical methods. All the samples were found to be contaminated with total viable bacteria and fungi with a maximum load of 103 cfu/ml among all samples were exceeded the United States Pharmacopeia (USP) limit (<102 cfu/ml). While the presences bacteria including; E.coli, Salmonella spp., Shigella spp., were found to be presences in almost all samples, (the former of E.coli in 11 syrups and suspension samples, the Salmonella spp. in 3 suspension samples and the Shigella spp. In 8 suspensions). Existence of microorganisms in the oral liquid samples might explain the treatment complicacy of the diseased children. A routine microbiological study of such drugs is thus suggested.

Keywords: Oral Drugs; Syrups; Suspensions; Microbiological Quality

Abbreviations: USP: United States Pharmacopeia; NAFDAC: National Agency for Food and Drug Administration and Control; GMP: Good Manufacturing Practice; HPMC: Hydroxy Propyl Methyl Cellulose.

Introduction

Microbial contamination of non-sterile products has become one of the main causes of product recalls and production halts at the start of the twenty-first century. Up to this point, microbial contamination of non-sterile pharmaceutical liquid goods is quickly growing into a worry for the entire world. Given that oral liquid medications must attain the highest level of sterility as required by their nature [1]. Unfortunately, due to their sweetening agent content, reconstitution techniques, improper storage, and handling defects, emulsions and syrups used for children are at a greater risk of microbial contamination during consumption. This could ultimately cause secondary and fungal infections in these patients. This suggests that microbial contamination of common medications is evolving into a public health issue [2].

According to the United States Pharmacopoeia (USP), liquid medications shouldn't include more than 103 colonyforming units of bacteria per milliliter (cfu/ml),

whereas yeast and mold shouldn't have more than 102 cfu/ml. The basic microbiological requirements for the certification of Syrup oral, suspensions were also described in the National Agency for Food and Drug Administration and Control (NAFDAC) Handbook (200). Therefore, the normal viable and fungal count for yeast and bacteria cells must not exceed 1.0x102 and 1.0x103 cfu/ml, respectively, for bacterial and fungal growth. In fact, cough syrups, paracetamol syrup, and antacids are the three most used oral liquid formulations (amongst other).Given their widespread commercialization and consumption in Nigeria, their microbiological safety is a significant public health problem [3]. Due to a variety of microbial growth effect parameters, such as poor good manufacturing practice (GMP) and carelessly implemented overall quality management, microbial propagation into pharmaceutical products is not improbable (TQM). Particularly in indigenous pharmaceutical industries in poor nations [4]. Unhygienic handling of medications in oral dosage forms, which accelerates the growth of a variety of bacteria and fungi within these non-sterile drugs, is the main cause of the unfortunate fatality that occurs due to medical complications that affect a great number of children in developing countries.

For pediatric patients, oral liquids such syrups, suspensions, emulsion, and aqueous solutions are employed. (USP) United States Pharmacopoeia (2003). Due to their high sugar and moisture content, these medications may serve as a favorable habitat and even a source of nutrition for the growth and survival of both pathogenic and non-photogenic microorganisms.

According to Nirmala, et al. [5], the quality of drugs in local pharmaceuticals varies greatly in Bangladesh and the majority of them are poorly made. Contaminated raw materials and manufacturing water that contains microbial bio burden or pyrupgens could be a beneficial source of bacterial and fungal contaminations in the pharmaceutical product. In addition, because of state legislation regulations, many unlicensed and illegal pharmacy stores sell pharmaceutical items that are shoddy made. For the safety of consumers, constant inspection of the microbiological quality of the products obtained from such stores is crucial.

The commonly used antacid suspensions in Bangladesh contain aluminium hydroxide, magnesium hydroxide & simethicone, or magaldrate preparation as primary ingredients, and these substances are susceptible to microbial spoilage as a result of low-cost manufacturing processes as well as inadequate storage and distribution methods [6]. The environment, raw materials, and manufacturing water used in the production of pharmaceuticals may contribute to the end products' microbial deterioration. A routine check for microbiological contamination of pharmaceutical products is necessary to assess the product quality and lower the risk to the public health in addition to in-process quality control and microbiological regulation of raw materials and final products [4]. In this vein, the goal of the current study was to assess the existing situation regarding these over-the-counter antacid suspensions produced by several national pharmaceutical companies in Katsina city.

The identification and quantification of microorganisms in oral pharmaceutical products are receiving more attention as a result of the rising number of patients with immune system impairments. The significance of microbial isolates other than primary pathogens and/or those in product monographs is therefore evaluated by manufacturers of non-sterile oral pharmaceuticals using a systematic approach while taking into account the number of organisms present, the type of dosage form, and the potential hazard to the user. Patients with immune system deficiencies are more susceptible to microbial infections, so the limits for objectionable microorganisms in oral products intended for immune compromised patient populations, such as children and cancer patients, should be stricter than the limits for oral products intended for treating patients with diseases or conditions that do not affect the immune system. When resistance mechanisms are compromised, whether by a severe underlying disease or the use of immunosuppressive medications, fewer opportunistic infections become contagious.

Literature Review

Syrup and Suspension

Syrup and suspension are the two primary liquid pharmaceutical formulation types (and variations of each). It assumes that when you say "syrup," you mean a solution. When the drug is taken, the solute in a solution is totally dissolved. The solute does not entirely dissolve in a suspension. As a result, a suspension has particles that are dispersed unevenly. When a medication cannot be entirely dissolved into solution, a suspension may be used to deliver a greater dose of the drug [7]. The only practical distinction when providing these medications is that a suspension must be shaken to evenly spread the product before administration, but a solution does not require this because the product is already uniformly dispersed because it has been dissolved in the solvent (though there are suspensions with other ingredients to suspend the particles more evenly). Most over-the-counter medications are solutions, and the most frequently used suspensions for children are different liquid form antibiotics, which must be mixed before use [8]. There are subcategories of these, such as "elixers," which are often solutions containing ethyl alcohol, and "emulsions," which are suspensions of two liquids that are insoluble in one

another. An emulsion would be similar to a salad dressing made of oil and vinegar that separates and needs to be mixed briskly. An "emulsifier," which aids in suspending the liquid droplets within the other liquid, is typically used to stabilize pharmaceutical emulsions [7].

For various diseases, we provide a wide variety of suspensions and syrups. Akemi, et al. [9] created a spray congealing approach for the taste of clarithromycin and discovered that the ratio of glyceryl monostearate and aminoalkyl methacrylate copolymer to clarithromycin produced better results. 2011's Hiroyo, et al. [10] Indelozagine hydrochloride, a bitter drug powder, was studied to determine how to make it taste better using a mixture of hydrogenated oil and a surfactant in a fluidized bed dryer. The side spray method revealed that heating the coated particles at a temperature above the melting point of a surfactant in the coated layer caused a notable increase in dissolution rate. By using the complexation technique and ion-exchange resins, Geeta Rao, et al. [11] developed a taste-masked oral suspension. The suspension was examined, and stability studies revealed no discernible change in the suspension. Release studies showed complete drug release within 20 minutes.

Suspension

It may be defined as a coarse dispersion of finely subdivided insoluble solid drug suspended in a suitable liquid (usually aqueous) medium. It is a heterogeneous system consisting of a solid disperses in a solid, liquid or gas. It is a biphasic preparations particle of one or more solids basically it may be flocculated or deflocculated [12].

Oral Suspension

It contains one or more active ingredients suspended in a suitable vehicle. Suspended solids may slowly separate on keeping but are easily redispersed. It should be packed in wide mouth bottles.

Formulation of Suspensions

A variety of things need to be considered while creating a suspension formula. First, a choice must be made regarding whether to evolve a flocculated or non-flocculated system. Second, it's crucial to make sure that the particles from the disperse phase are evenly dispersed in the continuous phase. The choice of suspending agents, dispersants, organoleptic additives, and preservatives must then be made in order to produce a satisfactory suspension [13]. The use of the products, the facilities for preparation and the length of product storage all affect the choice of an acceptable suspending agent.

Evaluation of Suspensions

A number of procedures have been suggested in the past for evaluating the physical stability of suspensions. Some of these are empirical in the sense that they have no mathematical base. Some methods currently being used are so drastic that they destroy the structure of suspension. The methods used may be categorized as;
Sedimentation methods
Rheological methods
Electro kinetic methods
Micrometric methods

Taste Masking

Many patients have trouble swallowing medications, especially youngsters and elderly patients when the tablets are large. Decide on oral dosage instead. After being taken internally, several medications leave a bad taste in the throat. Therefore, several substances are revealed that, when included in the formulation, can hide these harsh tastes [14]. The conventional oral dosage forms possess sustained release anti – tussive characteristics. Standard oral dosage forms have sustained release anti-tussive properties. The formulation of microcapsules allows for immediate, rapid release in the stomach and they are made into chewable, flavor-masked oral tablets or capsules. A copolymer of polymethacrylic acid and acrylic acid esters can make up the methacrylic acid copolymer. When using microcapsule techniques, these polymers' coating should be used for their immediate release properties [15].

A lot of medications with amine, amide, or salts thereof frequently taste very bitter. Techniques for concealing the taste with different sweeteners, amino acids, flavors, and adsorbents haven't proven successful. The majority of coating methods lack a reliable in-vivo drug release mechanism. For prolonged release action and flavor masking, cat ion exchange resins have been employed to adsorb amine medicines. The two most popular cat ion-exchange resins are polymers of sulfonic and carboxylic acids [14]. There are many different delivery methods being developed for various routes of administration, including oral, parenteral, nasal, and transdermal. However, the oral route remains popular for drug delivery since it is a simple, practical, noninvasive, and well-known form of administration. Oral dose forms are created based on the drug's nature [16]. Liquid mixtures in the form of tablets, capsules, and liquid-filled capsules are the most typical oral dose forms. Depending on the desired therapeutic action, such as controlled, extended, or delayed release, the solid dosage forms are further changed.

Patients who were at the age extremes, such as young children and the elderly, frequently had trouble ingesting

solid dose forms like solutions, emulsions, and suspensions. When the drag has a highly unpleasant taste, these dosage forms typically result in perceptible exposure of the active medication ingredient to the taste buds, which is a very serious issue. The taste of highly bitter medications like quinine, barberin, antibiotics like ofloxacin & clarithromycin, and flavoring agents such as amino acids, are frequently unmasked by conventional taste masking strategies such sweeteners, amino acids, and flavoring agents [16]. Taste masking is a significant issue when the drugs are very unpleasant. This issue is not only present in liquid oral compositions like solutions, dry syrups, and suspensions; it can also arise when chewable tablet dosage forms are created, as these dosage forms typically result in perceptible exposure of the active ingredient to taste receptors. Different strategies have been used to get around the drug's disagreeable taste and bitterness depending on the type of dosage form.

Ion exchange resins, complexing bitter medications with pharmaceutically acceptable receivers, coating drugs with lipids utilizing a variety of polymeric materials, and other methods for masking taste have all been tried in the past. The coating is the taste-masking method that is most frequently utilized. Any of the art's techniques, including microencapsulation, can be used to coat the active substance [17]. The use of ion exchange resins to absorb medications containing amino groups for taste masking has found limited application in masking the taste of medications that are extremely bitter, as well as in situations where the medications are to be dispersed in a liquid oral composition for a prolonged period of time. Tablets that dissolve in the mouth provide another method. This method calls for the disintegration of the substance in the oral cavity with saliva in 15 to 60 seconds without the need of water and with a satisfying mouthfeel. The two techniques were used to create mouth-disintegrating tablets. Sweeteners and disintegrants can be added [17].

Mass Extrusion Technique

In order to cover up an unpleasant taste brought on by the presence of a dissolved or suspended pharmacologically active chemical, these taste-masking formulations are typically flavored, such as with fruit or mint flavors. When the formulation is meant to be consumed by kids, a good flavor is especially crucial. the typical flavors that are frequently incorporated into formulas. Several additional flavors, including grape, cirus, peach, strawberry, and peppermint, are also significant flavors. Tokuwu, Sucralose and saccharin, two artificial sweeteners not based on sugar, are utilized in these formulations. Typically, water, alcohols, and glycerin are employed as suitable pharmaceutically acceptable solvents and or transport systems.

In the formulations, suitable buffering systems are also utilized. These buffer systems consist of citric acid and phosphoric acid. Preferably, sodium citrate is included in the citric acid buffer system together with citric acid. These compositions maintain a PH range of 4.5 to 6.5, preferably 5.5. These taste-mapping formulas use suitable thickening agents, such as xanthan gum, guargum, gelatin, taragum, tracaganth gum, and many more [18]. To stop microbiological contamination, preservatives such sodium benzoate (0.1 to 0.2%) or benzoic acid are utilized in these taste-masking formulations. Additionally, stabilizers should be added to the taste-masking formulations at concentrations of 0.01 to 5%, ideally 0.25 percent.

Techniques Employed For Taste Masking

The methods commonly employed for achieving effective taste masking include various physical and chemical methods that prevent the drug substance from interaction with the taste buds.

Use of Flavor Enhancers: Depending on the primary taste that is being concealed, the materials used for taste masking have frequently been categorized. Both natural and synthetic sources can be used to create flavorings and fragrances. Fruit juices, synthetic products like peppermint and lemon oils, aromatic oils, herbs, spices, and distilled fractions are examples of natural products. They can be purchased as syrups, spirits, alcoholic or aqueous solutions, or concentrated extracts. Numerous compositions, such as alkaline earth oxide, alkaline earth hydroxide, or an alkaline hydroxide, have been reported to exhibit efficient taste masking abilities with better flavor in addition to these typical materials [14].

A different composition contains mixes of phosphorylated amino acids such phosphotyrosine, phosphoserine, and phosphothreonine. Zinc, which is used to treat the common cold, has a bitter taste that anethole effectively masks. When used in formulations that are meant to be chewed or dissolved in the mouth before consumption, clove oil and calcium carbonate have been found to be especially effective at masking the unappealing active ingredients.

Applying Polymer Coatings: Coating of drugs using a suitable polymer offer an excellent method of concealing the drug from the taste buds. The coated composition may be incorporated into much number of pharmaceutical formulations, including chewable tablet, effervescent tablets, powder and liquid dispersion. Multiple encapsulated flavour delivery systems have been developed which is useful in chewing gum, pharmaceutical preparations as well as other food products [19].

Complexation and Adsorption Approaches Complexation with ion exchange Resins and Polymers: Cat ion-exchange resins CRP 244 and anion exchange ion were used to adsorb ester drugs for both masking of bitter taste and achieving sustained release action. The types of ion exchanges resins that have been successfully used to mask the taste of bitter drugs include amberlite IRP 88 (an acrylic potassium resin), amberlite IRP 64 (a polystyrene sulphonate) and amberlite IRP64 (a carboxylate form of the methapyrilene, dextromethrophan, ephedrine and pseudoephedrine) were masked by first forming adsorbates with polymethacrylic acid ion exchange resin followed by coating of resin complex with 4:1 mixture of ethyl cellulose and hydroxy propyl methyl cellulose (HPMC) polymers [20].

Prepared high potency adsorbents of methapyrilene, dextromethophan, ephedrine, pseudoephedrine by column procedures using a polymethacrylic acid ion exchange resin. Taste evaluation of the adsorbents showed a significant reduction in the bitterness of the drugs. Coating adsorbent particles with 4:1 ethyl cellulose HPMC mixture reduced the bitterness further. Taste coverage was maintained after incorporation of the coated adsorbent in to chewable tablets. Strong acid cat ion resins (sulfonated styrene divinyl benzene copolymer product) can be used for masking the taste of basic drugs. Polystyrene matrix cat ion exchange resins have been used to mask the bitter taste of chlorpheniramine malate, ephedrine hydrochloride and diphenhydramine hydrochloride. Extreme bitterness of quinolones has been achieved by ion exchange resin such as methacrylic acid polymer cross linked with divinylbenzene [21].

Drug Resin Complexes

When an ionizable drug reacts with a suitable ion exchange resin, the drug resin complex formed is known as a drug resinate. Since the drug resinate is insoluble, it has virtually no taste, so that even very bitter drugs lose their taste when converted into a drug resinate with the correct selection of the ion exchange resin.The drug resinate can be made sufficiently stable that it does not break down in the mouth so that the patient does not feel the taste of drug when it is swallowed. However, when the drug resinate come in contact with gastrointestinal fluids, usually the acid of the stomach. The complex is broken down quickly and completely. The drug is released from resinate directly into the solution and then absorbed in the gastrointestinal tract without being absorbed [22].

Formulation of Inclusion Complex with Beta Cyclodextrin Derivatives

Cyclodextrin are cyclic oligomers of glucose. They form inclusion complexes with any drug whose molecules can fit to the lipophile seeking cavities of the cyclodextrin molecule. The resulting complexes can marked improve the coating with suitable lipids, such as palmitic or stearic acid, glyceryl tripalmitate, glyceryl tristearate or a mixed acid ester triglyceride and stearyl alcohol [23].

Wax Embedding of Drugs

Taste masked by wax embedded granules of ephedrine hydrochloride, chloropheniramine maleate and Diphenhydramine hydrochloride were prepared in stearic acid and other waxes.

Other Techniques

These include solubility-limiting methods incorporation of drugs in vesicles and liposome and chemical modification. The solubility limiting method can be applied to a number of drugs whose taste profiles are dependent on aqueous solubility.

Chemical modification such as derivatization or lipophillic counter ion selection may be an effective method for reducing aqueous solubility and taste. Erythromycin monohydrate, a bitter tasting drug with a solubility of 2 mg/ml is chemically converted into erythromycin ethyl succinate, the aqueous solubility is reduced to the <50mcg/ml. This form is tasteless and can be administrated as a chewable tablet. Incorporation of drugs into Vesicles or liposomes is although an ideal technique. Yet a challenge to formulate without altering the regulatory status of the product (in-vitro dissolution kinetics, physical or chemical stability or bioavailability) [24].

Anesthetizing agent like sodium phenolate, which numb the taste buds sufficiently within 4-5 seconds is helpful in inhibiting the perception of the formulation. Substances like lipids, carbohydrate, lecithin, gelatin and polyamines has been effectively used for taste masking of drugs. Another novel technique employing mulitiple emulsions has also been reported. By dissolving drug in the inner aqueous phase of w/o/w emulsion under condition of good shelf stability, the formulation is designed to release drug through oil phase in the presence of gastric fluid [24]. In one of the method drugs with bitter taste are combined with non-ionic surfactants to form composites by hydrophobic interactions resulting in taste masking.

Techniques Employed For Taste Masking of Different Dosage Forms

The drug i.e. the active pharmaceutical ingredient is finally formulated in a suitable dosage form such as tablet, powder, liquid, etc.

Tablets: Most of the tablets can be effectively masked for their taste by applying inert polymer coatings that prevent the interaction of the drug substances with the taste buds. Nevertheless, attempts have been made time and again by several workers to investigate and explore the use of newer materials in bad taste abatement and good taste enhancement [25].

Granules / Powders: Granules for reconstituting as liquids (e.g. sachets, sprinkle capsules & powder) hold a high share of pediatric and geriatric market. A large number of patients on the topic highlight the significance of the same. Thus taste masking of granules becomes an important priority in product development and varied technologies and methodologies [24].

Liquids: They present major challenges in taste majority of pediatric preparation are syrups and suspensions although, the aforementioned methodologies have also had been used for improving liquid taste and few patents in this area are worth mentioning [14].

Sample Collection: The syrup and suspension ware collection from Dan guruff medicinal patients neigher by MTN office Kofar Kaura, Katsina state.

Material and Methods

Study Area

This research work was carried out in Katsina metropolis, Katsina state covers an area of 23938, 59km and is located between latitude 11° 08^1 N and 13°22^1 N and latitude 6° 52^1E.The state is bounded by niger republic to the north, Jigawa and kano state to the east Kaduna state south and Zamfara state to the west katsina state forms part of extensive plains known as high plains of hausa land. (Nigerian online©2005).The climate of the study area can be divided in to two zones climatically tropical and semi-arid continental. The south of the state from Funtua to dutsin-ma belong to the summer with the total annual rainfall figures ranging from 1000mm around funtua to over 800mm around dutsin-ma (www.google.com).The north of Katsina state from Kankia to the extreme north east has total rainfall figures ranging from 600-700mm annually generally climate varies considerably according to month and seasons, the area is cool-dry (harmattan) season from December to February, a hot dry season from march to May and warm-wet season from June to September. A less marked season after rains during the month of October to November. Characterize by decreasing rainfall and gradually lowering of temperature (Nigeria online.com©).

Preparation of Medium of Bacteria and Fungi

28g, 39g and 46g, of Nutrient agar, salmonella shigella agar, EMB agar and Potato dextrose agar ware weight respectively and dissolved in 1000ml of distilled water and sterilized using autoclave at 121°c for 15 minutes. And then 30ml of each of the media were poured into the Petri dishes respectively and allowed it to solidify. 1ml of each sample were measured and we're taking into test tubes before serial dilution was carried out in the following concentration 10^1 and 10^2, 1ml from each of the dilution was introduced into 9mm diameter petri dishes respectively, the petri dishes were then incubated at 37°c nutritient agar, salmonella shigella agar and EMB agar for 24 hours, and potato dextrose agar at 25°c for 72 hours. On the 24 hours, the plates were examined for microbial and fungi contamination and number of colony forming units (cfc) were counted using stuart sciencfic colony counter [26].

Total Viable Aerobic Bacterial Count

Viable aerobic mesophilic bacterial count was evaluated using pour plate method [26]. In this method, 1 ml of the sample was added to 20 ml of the liquefied casein soya bean digest agar at about 45 0C in a Petri dish. At least 2 Petri dish for each level of dilution were used. The plates were incubated at 30 – 35 0C for 5 days, unless a reliable count was obtained in a shorter time. Suitable dilutions yielding < 300 colonies were counted. The arithmetic mean of the counts was taken and number of colony forming units per gram or milliliter (cfu/g or mL) was calculated.

Detection, Isolation and Identification of Potential Aerobic Bacteria

An aliquot (1 ml) of the supernatant (for tablets) or 1 ml of each liquid dosage product was spread on nutrient agar, blood agar, MacConkey agar and mannitol salt agar plates. All plates were incubated at 37 0C for 24 h. The colonies produced were examined morphologically, microscopically and biochemically. Morphological identification was based on size, diameter, elevation, translucency, color, etc. of the colonies formed while microscopical identification was achieved by spreading the bacteria on a microscope slide and examined under a microscope after Gram staining to identify Gram- and –negative bacteria. For biochemical identification, a number of biochemical tests including carbohydrate utilization, catalase production, oxidase production, tests, methyl red, Voges-Proskauer, nitrate reduction, starch hydrolysis, tryptophan hydrolysis, hydrogen sulfide production, and citrate utilization were carried out.

Detection, Isolation and Identification of Fungi

One milliliter of the test supernatant (for tablets) or of the test liquid product was spread on *Sabouraud* agar plates. The plates were incubated at 25 – 27°C for 72 – 96 h and fungal growth were examined both macroscopically and microscopically.

Determination of Sodium Nitrite of Precetamol

Standard Preparation

0.114g of sodium Nitrite standard was weight into 100ml volumetric flask, and dissolve with sufficient water and make up to mark.

Analiyte Preparation

10ml of cough syrup was measure into 100ml volumeric flask and diluted with water and made up to the mark.

Procedure

5ml of each of the standard, analyte solution above was measured into 250ml volumetric flask. 10ml of Hydrochloric acid solution was added into each standard and analyte. 5ml of sodium Hydroxide solution (in 0.1M Hydrochloric acid Solution) was added into each. Blank was prepared with 5ml of the without analyte Sodium hydroxide solution. Standard, analyte and blank was diluted all to 25ml with 0.01M Hydrochloric acid solution. Absorbance of standard, analyte and analyte blank solution was mix and measured @ 520nm [26].

Calculation

Corrected analyte absorbance = Absorbance of analyte - Absorbance of analyte blank

$$Qty\ of\ sodim\ citrate = \frac{Absorbance\ of\ sample\ \ x\,0.114\,x\,125}{Absorbance\ of\ standard\ x\,0.114}$$

$$Assay\ of\ sodim\ citrate = \frac{Qty}{125}\,x\,100$$

etermination of Assay Contents of Ampicillin and Amoxicillin Suspension

Ampicillin Suspension

2gm of Ampicillin dry syrup was weight blend / 10ml was reconstituted powder into 250ml conical flask. 50ml of distilled water was poured into the blend / syrup and was shake. The solution was dissolve with the aid of gentle heat on water bath for 20 minutes. The solution was allowed to cool. 2 drops of phenolphthalein solution was added into the content of the conical flask. The solution was titrated with 0.1M of NaOH. The titrated value obtained is for Ampicillin value calculation. And each of 0.1M Sodium hydroxide is equivalent to 34.95mg of Ampicillin [26].

Calculation for Ampicillin

$$Qty\ of\ active\ ingredient = \frac{Titre\ value\ x\ factor\ of\ 0.1M}{2.0\,x\,0.1}\,x\,43.52$$

$$Assay = \frac{Qty}{125}\,x\,100$$

Amoxicillin Suspension

2gm of Amoxicillin dry syrup was measure 10ml reconstituted powder into 250 conical flasks. 50ml of distilled water was into the blend / syrup and was shake. 50ml of 0.1M NaOH was added to the final solution. 50ml if NaOH was poured into a conical flask for the blank. Both the test solution and the blank were carried on water bath and heat for 1 hour. The solution was allowed to cool. 2 drops of phenolphthalein solution was added into the blank solution. The blank solution was titrated with 0.1M of HCl. 2 drops of phenolphthalein solution was added into the test solution and titrated with 0.1M HCl. Each ml of 0.1M sodium hydroxide is equivalent to 43.5mg of Amoxicillin [26].

Calculation for Amoxicillin

For Amoxicillin titre value

Amox titre value = Blank titre - test titre = Different (y)

Amox titre value = Different (y) - Ampicillin = Amox

$$Qty\ Amoxicillin = \frac{Amox\ titer\ \ factor\ of\ 0.1M\ \ NaOH}{2.0\,x\,0.1}\,x\,43.5\,x\,2$$

$$Qty\ of\ \ sodim\ citrate = \frac{Absorbance\ of\ \ sample}{Absorbance\ of\ \ standard}\,x\,wiegnt\ of\ \ sample$$

$$\%\,Assay\ of\ \ sodim\ citrate = \frac{Qty}{2.0\,x\,0.1}\,x\,100$$

Determination of the Assay Contents of Cough Syrup

Composition

Each 5ml of cough syrup contains: 135mg of Ammonium chloride BP; 57mg sodium citrate BP

A. Ammonium Chloride

Procedure: 5ml of the cough syrup was measure into a conical flask. 20ml of water into conical flask was raised the pipette. Another 20ml of water was added and shake. 20ml of previously neutralized formaldehyde solution was added into

the sample (20ml formaldehyde was separated in a conical flask, 2 - 3 drops of phenolphthalein solution was added and titrated with 0.1M sodium Hydroxide to a pink end-point). Sample was titrated with 0.1M sodium Hydroxide solution by using a further 2 - 3 drops of phenolphthalein solution as indicator. Each ml of 0.1M sodium Hydroxide solution is equivalent to 5.349 mg of Ammonium chloride [26].

Calculation

$$Qty\ of\ Ammonium\ cholride = \frac{Ttite\ value\ x\ equivlent\ wt.x\ factor\ of\ titre}{Molarity\ of\ titrant}$$

$$Assay\ of\ Ammonium\ chloride = \frac{Qty}{135} x100$$

Sodium Citrate

Standard Preparation: 0.114g of sodium citrate standard was weight into 100ml volumetric flask, and was dissolve with sufficient water and was make up to mark.
Analiyte Preparation: 10ml of cough syrup was taking into 100ml volumeric flask and diluted with water to mark.

Procedure

5ml of each of the standard, analyte solution above was taking into 250ml volumetric flask. 10ml of Hydrochloric acid solution was added into each standard and analyte. 5ml 0.5% w/v Ferric chloride solution (in 0.1M Hydrochloric acid Solution) was added into each. Blank was prepared with 5ml of the analyte without Ferric chloride solution. Standard, analyte and analyte blank was diluted all to 25ml with 0.01M Hydrochloric acid solution. Absorbance of standard, analyte and analyte blank solution was mix and measured@380nm [26-28].

Calculation

Corrected analyte absorbance = Absorbance of analyte - Absorbance of analyte blank

$$Qty\ of\ sodim\ citrate = \frac{Absorbance\ of\ sample}{Absorbance\ of\ standard} x\ wiegnt\ of\ sample$$

$$Assay\ of\ sodim\ citrate = \frac{Qty}{57} x100$$

Results (Table 1&2)

Sample type	Sample name	T. Aerobic count (cfu/ml)	T. Fungal count (cfu/ml)	E. coli	Salmonella spp.	Shigella spp.
Paracetamol syrup	Tuliy	1.3×10^2	8.0×10^2	+	-	-
	Labc Avro Archy	7.6×10^2	1.8×10^2	+	-	-
	Phamtex	8.0×10^2	4.8×10^2	+	-	-
	Avro Archy	1.8×10^2	1.2×10^2	+	-	-
		2.8×10^2	4.0×10^2	+	-	-
Cough syrup.	Totulin	5.0×10^2	3.4×10^2	+	-	-
	Greelin	5.6×10^2	4.4×10^2	+	-	-
	Tuxili-N	1.9×10^2	8.0×10^2	+	-	-
	NGC	6.8×10^2	4.0×10^2	+	-	-
Amoxicillin suspension.	Tuliy	7.2×10^2	8.8×10^2	+	+	+
	Impact	3.2×10^2	1.1×10^2	-	+	+
	Geneth	8.0×10^2	9.6×10^2	-	-	-
	Ac. Drugs	6.0×10^2	2.5×10^2	-	-	+
Ampicillin suspension.	GSK	2.6×10^2	8.0×10^2	-	-	+
	Ac. Drugs	1.8×10^2	Nil	+	-	+
	Kapiclox	9.6×10^2	1.2×10^2	-	-	+
	Jawa	1.4×10^2	2.0×10^2	-	-	+
	Tuliy	8.0×10^2	3.2×10^2	-	+	+

Table 1: Microbial load in the syrup and suspension tasted.
Key points: present (+). Absent (-).

Sample type	Sample Name	pH	Assay Content (%)
Paracetamol syrup	Tuliy	5.5	111
	Labc	6.8	14
	Phamtex	4.6	104
	Avro	5.1	14
	Archy	5.6	13
Cough syrup	Totulin	5.6	101
	Greelin	3.6	100
	Tuxili-N	4.5	100
	NGC	5.4	100
	Tuliy	6.2	23
Amoxicillin suspension	Impact	5.5	33
	Geneth	5	26
	Ac. Drugs	5.5	33
Ampicillin suspension	GSK	4.7	32
	Ac. Drugs	5.9	42
	Kapiclox	6.2	27
	Jawa	5.4	7
	Tuliy	5.6	15

Table 2: Determination of PH and Assay contents of syrup and suspension.
Keys: pH = 4.0 – 7.0, Assay Content(s) = not more than 105

Discussion

Table 2.1 show the results of total aerobic count from all the syrups and suspensions tested. High bacteria count of (8.0×10`2) was observed in paracetamol syrup from Phamtex pharmaceutical while the lowers count of bacteria of (1.3×10`2) was observed in Tuliy pharmaceutical. All the syrups and suspensions samples used in this study were still within their shelf-life when the analysis was carried out. This study revealed that only few syrups and suspensions we're contaminated microbiolocally. The isolated aerobic bacteria in paracetamol syrups were *E.coli* and that of suspensions were *E.coli* and *Salmonella-Shigella* spp. and total Coliform. All the paracetamol syrups analyzed are free from *Salmonella-Shigella* spp. The presences of this bacteria like *E.coli* and *salmonella-shigela* spp is significant as they may cause potential determination in the health status of the patients particular those that are immunological compromised and infant's with immature Immune system. This contamination of the cough syrup and paracetamol syrup may be attributed to poor manufacturing practice, air in the manufactory environment, from raw materials, water used personnel, packaging process or containers and equipment. The presence of *E.coli* and total coliform in some of the Cough Syrups and Paracetamol syrup samples indicated fecal contamination that may be from production personnel through water as vehicle. *Escherichia coli*is an ideal indicator organism to test samples for fecal contamination as they are not always confined to the intestine and able to survive for brief period outside of the body. The Microbiological analysis of the samples showed compliance with (USP) official requirement of Microbial load of the (50.00%) samples was within the USP permissible limits for non-sterile Pharmaceutical products.

Conclusion

In conclusion, the result shows the microbial contamination of some selected syrup and suspension sold in katsina state. Therefore, presences of any microorganism should be considered undesirable for all drugs. Although specific Gram - negative enteric bacteria we're not found in the tested samples, presence of viable bacteria especially Gram - positive one along with fungi claimed a sort of public health risk associated with the consumption of those drugs. The compliance sectors among the Nigeria pharmaceutical should strictly deal with Microbial stringency within the manufacturing, packing, distribution and storage of pharmaceutical products present situation might be global significance in terms of public health measure and hence, a regular micro examination of oral drugs in suggested, especially in the developing countries.

Recommendation

In order to reduce or avoid contamination of pharmaceutical products, it is therefore pertinent to make the following recommendation.

- All raw materials used particularly water and other materials used as suspending agents and ingredients should be of high microbiological safety standard.
- All apparatus or processing equipment used should be subject to planned preventive maintenance and should be properly cleaned and sterilized after use to prevent cross-contamination between batches.
- During packaging of the end-product, proper care should be taken to prevent contamination and reduction of its shelf-life.
- Pharmaceutical products should be stored in a cool and dry place, with syrup stored at 4°c and suspension 25°c to avoid spoilage and degradation.

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