Detection of Fungal Contamination in Come Valid and Expired Gastrointestinal Drugs Produced By Some Pharmaceutical Companies in Libya North Africa.

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Abstract :

Purpose :To determine the type and incidence of predominant microorganisms in certain non-sterile pharmaceuticals immediately after collection and one year later. Objective: To determine the type and prevalence of microorganisms present in pharmaceutical preparations immediately upon collection .**Methods** :The following tests were performed on all pharmaceutical samples: Detection of fungi associated with expired and valid medicines using conventional techniquesThis study, conducted at Al-Mawakeb Institute during the academic year2024/2025, investigated fungal contamination associated with selected gastrointestinal medications. The drugs examined included Omeprazole 40 mg, manufactured by the Indian company Shifa_Ron, andCystone, produced by the Indian company Himalaya. Samples were collected from private pharmacies in the Yefren region, Libya.The **results** revealed the presence of *Candida parapsilosis*in 75% of expired Omeprazole samples when diluted at ratios of 1:10 and 1:1000 on Potato Sucrose Agar (PSA) medium. In the case of Cystone, isolated on Sabouraud Dextrose Agar (SDA), the following fungi were detected in the expired product :*Stemphylium* ,(%50)*Alternaria* ,(%40) *Aspergillus niger* ,(%5) and *Aspergillus candidus* .(%5) Additionally ,*Aspergillus niger* was found on PSA medium in 25% of Cystone expired samples.For the non-expired Omeprazole samples, direct fungal isolation on PSA showed the presence of *Penicillium* in 25% of samples, while on SDA, both *Alternaria spp* .and *Aspergillus spp* .were found in 50% of samples each. In non-

expired Cystone samples ,*Alternaria*was detected on PSA in 25% of cases.This is the first study conducted in the Yefren region to investigate fungal contamination in gastrointestinal medications.

Introduction

Contamination of pharmaceuticals with microorganisms irrespective whether they are harmful or nonpathogenic can bring about changes in physicochemical characteristics of the medicines. Although sterility is not a requirement in official compendia for nonsterile pharmaceuticals, bioburdens need to be within acceptable limits(Mugoyela and Mwambete.,2010) . Pharmaceutical products can be classified into two micro-biologically groups: sterile and non-sterile. The pharmaco-

poeial monographs specify what microbiological standards must be met for sterile and non-sterile drug (United States Pharmacopia.,2007) . Also, in the last three years, FDA recalled several drugs due to fungal contamination. For instance, on April 2021 and August 2020, FDA showed *Aspergillus penicillioides* contamination in ChloraPrep drugs, which Becton, Dickinson and Company manufacture. The manufacturer confirmed that the contamination of ChloraPrepTM 3 mL with *A. penicillioides* occurs if it is stored in regions that are extremely hot and humid for more than six months, where it may be consistently exposed to temperatures of 30°C and 75% relative moisture (*FDA 2020*, *FDA2021)* . Fungal contamination in gastrointestinal drugs poses significant public health risks, leading to severe infections and treatment failures. Contaminated pharmaceuticals can arise from inadequate compounding practices, improper storage conditions, and the presence of resistant fungal species. The following sections detail the sources, impacts, and implications of fungal contaminants in gastrointestinal drugs, Fungi play a significant role in the contamination of medicines, particularly in herbal and pharmaceutical products. Various species contribute to this issue, with notable prevalence in different contexts. The following sections outline the types of fungi involved and their respective presence in medicinal products (Denyer et al.,2011) Contaminated drugs can lead to invasive mycoses and other serious infections, particularly in immunocompromised patients (Khanet al.,2015). Pollution is broadly defined as the introduction of harmful substances or energy into the environment, which can adversely affect human health, ecological systems, and the

quality of natural resources. This definition encompasses various forms of pollution, including chemical, physical, and biological contaminants, and recognizes both human-made and natural sources. The complexity of pollution is highlighted by its classification into point source and nonpoint source categories, as well as its historical context, tracing back to early human activities. Pollution involves the introduction of contaminants that impair environmental functioning or pose risks to health. it can manifest as chemical substances, noise, light, or temperature changes. The definition reflects competing rationales for environmental protection, focusing on human health and ecological integrity (Kramer et al.,2006) .Pollution has existed since prehistoric times, with evidence of soot from early fires. The industrial revolution marked a significant increase in pollution levels, leading to notable events like the Great Stink in London. Pollution can be categorized into various types, including Chemical Pollution: Introduction of harmful chemicals into air, water, or soil. Biological Pollution: Involves pathogens or invasive species that disrupt ecosystems. Physical Pollution: Includes noise, light, and thermal pollution (Tavares et al.,2020) .Provided that the microenvironment within the final product is favourable, microbial contaminants can proliferate and colonize the product for a considerable amount of time until the product finally reaches the final consumer(Kramer et al.,2006;Khan et al.,2015.Microbial contaminants in pharmaceutical products beyond acceptable limits have detrimental effects on both the product manufacturer and consumers. It is widely known that microbial spoilage of pharmaceutical products may result in physicochemical deterioration of both the active and inactive ingredients of the preparation. Ultimately, less effective, or toxic constituents may be formed. The presence of microbes may also have a direct hazardous effect on the consumer's health by causing infections. Microbial contaminants, particularly on antimicrobial products, may give rise to resistant strains, contributing to antimicrobial resistance. In addition, microbial toxins also pose risks to the individual's health(Denyer et al.,2011;Kamil and Lupuliasa.,2011) .Massive outbreaks of medicine –related infections have resulted on several occasions (Jimenez.,2019; Tavares.,2022) Microbial contamination in pharmaceutical products, including gastrointestinal drugs, poses significant risks to patient health and safety. This contamination can occur at various stages of production, from raw materials to finished products, and can be attributed to

environmental factors, human error, or equipment-related issues. The presence of microorganisms such as, fungi, in pharmaceuticals can compromise the quality, efficacy, and safety of the products, leading to severe health implications for consumers (Hashim and Celiksoy.,2025)Expired medications pose significant risks to both human health and the environment. The prevalence of expired drugs in households is alarmingly high, with studies indicating that nearly half of homes store such medications, often leading to potential health emergencies due to accidental ingestion (Fernandes et al.,2020) Furthermore, improper disposal practices exacerbate these risks, contributing to environmental pollution and posing threats to wildlife and human populations(Nepal et al.,2020).Gastrointestinal (GI) drugs play a crucial role in managing various disorders affecting the digestive system. These medications are designed to normalize impaired GI function and address symptoms such as heartburn, dyspepsia, and nausea. The development of GI drugs has evolved significantly, with a focus on understanding their mechanisms and the challenges associated with gastrointestinal drug delivery. Below are key aspects of gastrointestinal drugs.. Antisecretory Agents: Includes proton pump inhibitors (PPIs) and histamine H2-receptor antagonists, which revolutionized the treatment of gastric ulcers and gastroesophageal reflux disease (GERD).Prokinetics: These drugs enhance gastrointestinal motility and are used in conditions like irritable bowel syndrome (IBS).Antiemetics: Medications such as ondansetron are effective in preventing nausea and vomiting, particularly in chemotherapy patients (Darand Dalton., 2007). Molds tend to grow at a variety of temperatures, from cold storage to those temperatures that are quite warm. It is common to find out that temperatures close to freezing (e.g., in a refrigerator) are not sufficiently cold to inhibit mold growth. Many believe that temperatures must be in the room temperature range (20°C to 25°C) for mold growth. In reality, molds grow quite well at 30°C to 35°C also. They can cause disease in humans, who have temperatures around 37°C. In fact, temperatures much warmer, like those in the tropics, are also conducive to mold growth (Hubka and Moldenhauer, 2015) The majority of molds require moisture and it can be necessary in sufficient quantities for growth. Typically mycologists refer to this moisture as water activity necessary for growth. The specific water activity level necessary is different for different species of mold. Most molds have levels that correspond to corresponding relative

humidity of at least 70%. Most major mold outbreaks occur where porous, cellulose-type materials have been kept wet by liquid water or sustained condensation (Anonymous, 2015). Water leaks provide. The objective of this study was to analyse samples of selected tablets, capsules, of imported non-sterile pharmaceutical products for microbial quality and quantity to provide a clue about conformity to GMP guidelines during manufacturing, storage.

Material and Methods

Study Site.

The study was conducted in the Microbiology Laboratory at Al-Mawakeb Institute for Medical Sciences and Medicines during January 2025.

Sample Collection

Samples of gastrointestinal drugs were collected from various pharmacies operating in the city of Yafran. The samples included both expired and valid medications, as detailed in the tables below.

Table 1. Expired Gastrointestinal Drugs

Drugs	Composition – Active Ingredients	Pharmaceutical forms	Company production	Date of Manufacture	Expiry Date
Omeprazole 40mg	Each hard gelatine capsule contains Omeprazole BP 40mg as enteric coated pellets	Capsules Bp	India ,Code No :MH/DRUGS/KD-671,Batch No :FO-02	8/2019	7/2022

Cystone	*Didymocarpuspedicellata 65mg,Saxifragaligulata49mg,Rubia cordifolia 16mg,Cyperus scariosus16mg,Achyranthes aspera (Apamarga) – 16mg,Onosmabracteatum16mg, Vernonia cinerea16mg,pdrus.Hajrulyahoodbasilicum,DolichosbiflorusmTribulusterrestrismomosapudicaodorata,Equisetum arvense, Tectona grandis*seed	Tablets	Himalaya Drug Company and Imported by Multipharma ,Egypt	9/2021	8/2024

Table 2. Valid Gastrointestinal Drugs

Medication	Active Substance	Date of Manufacture	Expiry Date
Omeprazole	Omeprazole	01/2024	12/2026
Cystone	.*Didymocarpuspedicellata (Shilapushpa) ……*	8/2023	7/2026

Preparation of Media culture :

The detection of microbial contamination in pharmaceutical products involves a range of methods, from traditional culture techniques to include the use of Sabouraud dextrose agar(SDA) and PDA for fungal growth, followed by morphological(**Brito**and Lourenço.,2021.

Preparation of SDA Medium Supplemented with Amoxicillin:

A Sabouraud Dextrose Agar (SDA) medium was prepared by accurately weighing 40 grams of SDA powder using a sensitive balance. The powder was transferred into a 500 mL flask, and 500 mL of distilled water was added. The mixture was heated over a gas flame with continuous stirring until the medium was completely dissolved. Once fully dissolved, the solution was allowed to cool slightly, then autoclaved at 121°C under 15 psi pressure for 20 minutes to ensure sterilization. After autoclaving, the flask was removed and allowed tocool for approximately 15 minutes until it reached a temperature suitable for antibiotic addition. A 500 mg amoxicillin capsule was opened, and its contents were added to the sterilized, cooled medium to inhibit bacterial growth. The mixture was gently stirred in a circular motion to ensure even distribution of the antibiotic. Finally, the medium was poured aseptically into sterile 9 cm Petri dishes and left to solidify at room temperature. *(***Alteyar***.,***2015***)*

Preparation of Potato Dextrose Agar

In this study, 300 grams of healthy potato tubers, which exhibited no visible symptoms of infection, were collected and carefully washed with plain water to remove any dust. The potatoes were then peeled to remove the outer skin and cut into small cubes, each approximately 4 cm in size. These potato cubes were weighed using a sensitive electronic balance (**model SF_400**, **produced by Sensor disc Technology Company**) with a weight capacity of 200 grams. The cut potato pieces were placed in a 1-liter glass flask, and 1000 ml of distilled water was added. The mixture was heated over a gasoline stove for 45 minutes to obtain an aqueous extract. Once the extraction process was complete, the solution was filtered through sterile cotton gauze to remove potato plant tissues. The filtered aqueous extract was then transferred to a clean container, and 15 grams of sucrose were added to it,

followed by thorough stirring. Next, 20 grams of agar-agar were added to the solution and stirred again to ensure a homogeneous mixture. This nutrient medium was heated over the gasoline stove until the solution was well mixed. The prepared solution was then sterilized in an autoclave at 121 °C for 20 minutes. After sterilization, the solution was allowed to cool to approximately 40 °C. Once cooled, 500 mg of Amoxicillin, produced by Pl Holder Brown Burk UK, was added to prevent bacterial growth. The solution was gently stirred in a circular motion to dissolve and thoroughly homogenize the ingredients, resulting in a final nutrient medium suitable for the cultivation of microbial cultures. The preparation method is based on established protocols for creating nutrient media for microbiological studies.) It was poured into plastic petri dishes size 9 cm produced by Aptaca. Italian S.P.A for 4 repeaters

Laboratory Procedures

Sample Preparation

Samples were randomly selected from available product packs of 50 tablets and capsules. The tablets and capsules were finely ground to homogeneous powders. 10 grams (for solid dosage forms) were accurately weighed per sample under sterile conditions to minimize the risk of external contamination. The samples were then diluted to 1:10 , 1:100 and 1:1000 dilutions for subsequent analysis.

identification of the Fungal Isolates

Morphological, methods were used for the identification of the isolates. The plates were examined for the presence of noticeable growth and once this is observed, the texture, pigmentation and topography of each specific type of colony was noted for proper and accurate identification. A little portion of the growth colony was teased with an inoculating needle and mounted on the slide with a drop of Lactophenol blue, covered with a cover slip. The preparation was examined under a light microscope with an attached camera (Motic Mc digital colored camera) connected to a computer for the microscopic photography of the fungi. The essence of this was to observe the exact arrangement of the conidiophores and the way the spores are produced. The identities of these fungi isolates were certified using cultural as well as morphological methodologies by comparing the isolates

with confirmed representatives of different fungal species in relevant texts before molecular identification for proper confirmation (Alexoupolous et al.,2007 ; Ellis et al.,2007).

Microbial Enumeration Test

Samples were examined using a surface-spread plate-count method. Using Petri dishes, 15–20mL of PDA medium (Accumix ®, Microexpress ® - India) for the cultivation of fungi and a liquefied Sabouraud Dextrose Agar (SDA) medium (HIMEDIA ®, HiMedia Laboratories- India) for the cultivation of fungi were added at about 45 °C to each Petri dish and allowed to solidify. The plates were dried in a hot air oven. A measured volume of0.2 mL of the samples prepared were spread over the surface of the media. Three Petri dishes (triplicates) wereused for each medium and each level of dilution. The plates wereincubated at 28°C, seven days for fungi unless a reliable count was obtained in a shorter time.The frequency of fungi in all dishes was then calculated according to the equation (Akhtar et al., 2007): Frequency percentage = number of fungal colonies ÷ total number of fungal colonies × 100.

Results:

Total Yeast and Mould Count (TYMC)

The results of isolating the accompanying fungi on the expired drug Omeprazoleexpired used for Gastrointestinal showed the presence of fungi *Candida .parapositosis* (Figure 1) at a dilution of 1:10 and 1:100 at a rate of 75% on the nutrient medium PSA as well as upon direct isolation.While the study showed the presence of fungi (Table,3) in different proportions on the nutritional medium SDA.the presence of fungiand found of fungi *Aspergillus niger*:inPSA media .The results of isolating fungi associated with unexpired omeprazole in direct isolation showed the presence of fungi in different proportions on the SDA,PSA medium(Table,4) . and found fungus *Alternaria*spp ratio 25 % on tablet Cystoneunexpired

Table3.Contamination Breakdown by Organism on SDA Medium to Cystone:

Fungus	Ratio %
Aspergillus niger:	50
A. candidus	40
Alternariaspp	5
Stemphyliumspp	5

Table4. Ratio of fungus on different media by direct isolation to Omeprazole 40mg.

Media culture	Fungus	%
PSA	*Pencilliumdigitatum*	25
SDA	*Alternariaspp*	50
SDA	*Aspergillus flavus*	50

Characteristics of colonies of *Candida .paraposilosis*:

Candida parapsilosis is a fungal species of yeast that has become a significant cause of sepsis and of wound and tissue infections in immunocompromised (Trofa ET al.,2008)people.Colonies of *Candida parapsilosis* are typically Pink to creamy, shiny, and smooth, but can also be wrinkled on Chrom agar candida . They can appear smooth or cratered when in yeast form, while pseudohyphal colonies exhibit crepe or concentric phenotypes. The specific appearance can vary based on the growth medium and other factors. However, characteristics of *C. parapsilosis* that may relate to its increasing occurrence in nosocomial settings include frequent colonization of the skin, particularly the subungual space.

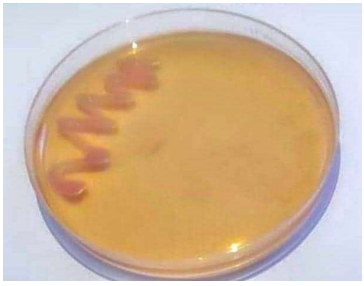

Figure1: growth yeast of *C.paraposilosis* on groom agar Candida

Characteristics of colonies of *Aspergillus niger*:

Colony is fast growing one ,black in colour ,conidial head is short ,conidophores is erect and simple with thick wall(Figure 2,B) .

Figure2: **A**. *growth Aspergillus niger*,on surface Tablet Cystoneand B, Microscopic characteristics

Characteristics of colonies of *Aspergillus candidus*:

Initial Growth: Colonies begin as white with a soft, velvety surface.On Sabouraud Dextrose Agar (SDA), colonies of *Aspergillus candidus* are characterized by their initial white, velvety surface, which later develops a raised, floccose center. During sporulation, the colonies produce yellowish-green and olive-colored conidia, and sclerotia may also develop, initially white and later turning brown (Figure ,3) .

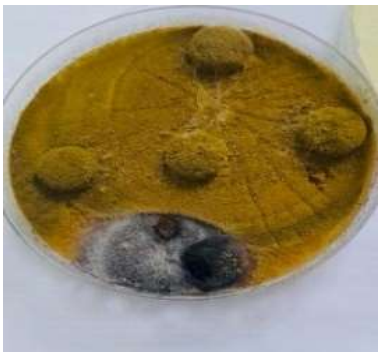

Figure. (3) :Colony morphology of isolate *AspergillusCandidus*on Sabouraud Dextrose Agar (SDA) on surface Tablet Cystone

Characteristics of colonies of *Stemphyliumsp*

*Stemphylium*sp colonies are typically rapid-growing, with a velvety or cottony texture. They can be various shades of brown, greyish, and often have a black reverse. Colonies on (SDA) are often woolly to cottony at 28°C (Figure,4) .

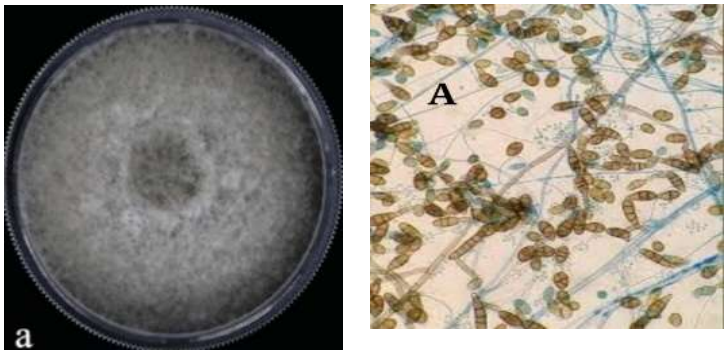

Figure4:a Colony morphology of isolate *Stemphyliumsp*and A ,conidial *growth*on Sabouraud Dextrose Agar (SDA) on surface Tablet **Cystone**

Characteristics of colonies of *Alternariasp*

*Alternaria*spcolonies are characterized by their gray to black color, suede-like texture, and ability to produce conidia in branched chains. These conidia are typically multicellular and have a "beak-like" apical cell. The colonies can range in color from olive-to-dark grey and are known for their rapid growth(Figure,5)

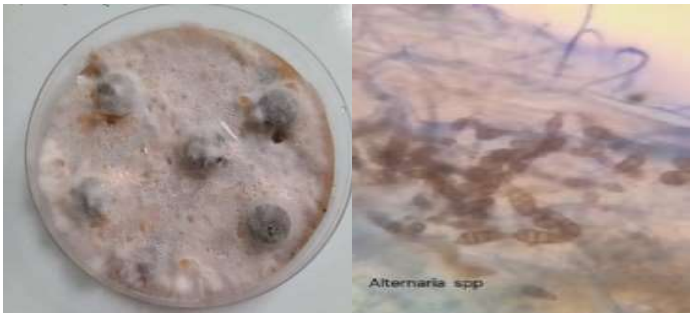

Figure5: a growth*Alternaria*spColony morphology of isolate *Alternariaspsp*and B ,conidial *growth* on Sabouraud Dextrose Agar (SDA) on surface Tablet **Cystone**

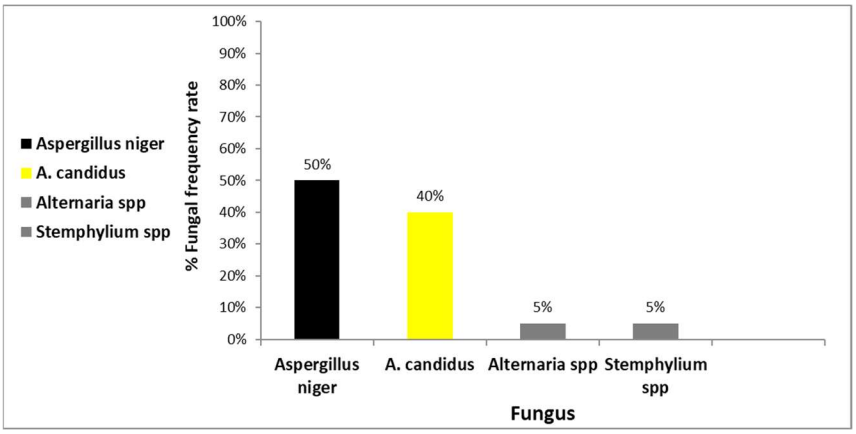

Figure6:A bargraph showing the frequency percentage of fungi on SDA medium .

Characteristics of colonies of *Pencilliumdigitatum*

Penicilliumdigitatum colonies are typically green, sometimes with white margins, and often exhibit a velutinous or velvety texture. They are fast-growing, particularly on media (PSA) potato Sucrose agar The colonies often produce a distinctive odor of decaying citrus fruit(Figure,6).

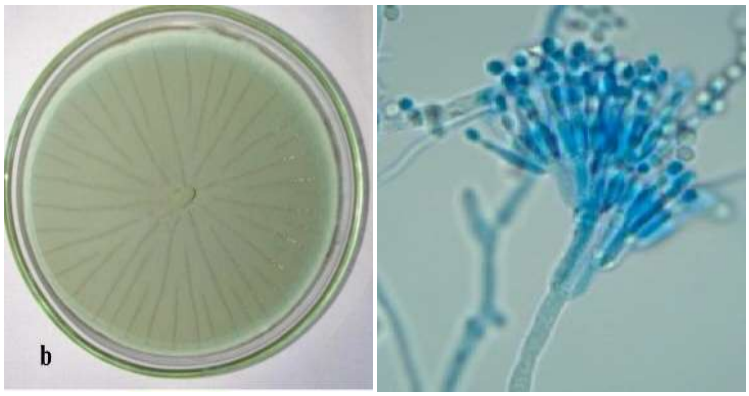

Figure5:a growth Green mold of*Pencilliumdigitatum*B ,Coniiophores

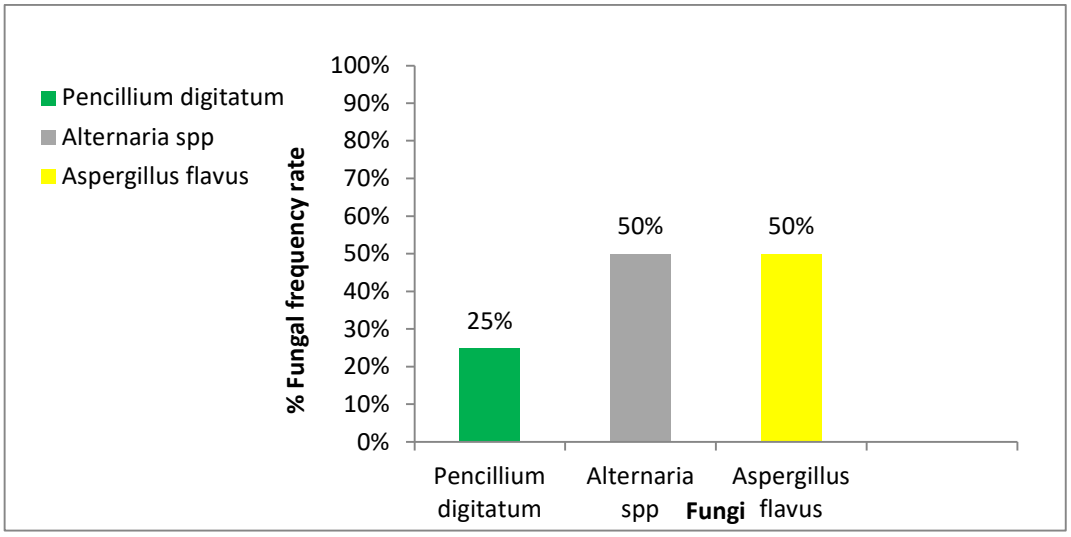

Figure 13: A bar graph showing the frequency percentage of fungi on PSA and SDA Medium

Discussion:

The result of study approvalwith results found(Anyanwu.,2010 ; Wang et al.,2024). to found *Aspergillus*sppCommonly found in herbal medicines, identified in 58.3% of samples from Enugu State *Fusarium* spp.: Predominant in herbal medicines, accounting for 27.74% of fungal isolates in a study from China [*Penicillium*spp: Present in 41.6% of herbal samples and known for producing mycotoxins*Alternaria*spp: Found in 20.81% of herbal medicines, also associated with mycotoxin production and most fungal ability production toxins caused decrease incidence diseases to humans .Aspergillus has beenidentified as the

causative agent of Aspergillosis infection which is a non contagious diseases that affect humans such allergic broncho-pulmonary aspergillosis and fungal,surhermore they emphasized that these mycotoxins can cause allergies acute and chronic poisoning liver damage and diseases of the respiratory and digestive system to high micomicrobialwth in pharmaceutical products (Parker .,2010 ;Najmuddin et al.,2010) .This study found the tested pharmaceutical products to be contaminated with microorganisms, albeit at different levels, with only one set of products Tablets and Capsule passing both tests for total aerobic microorganisms and total yeast and mold counts. High levels of contamination are undesirable for pharmaceutical products. Microbial agents may cause physicochemical degradation of the product, causing the formation of ineffective and/or toxic by-products,Meanwhile*Aspergillusflavus* followed by *Aspergillus*fumigatusand*penicilliumspp*were suspected among the fungal isolatcs, No *Candidaspp*or any other yeast cells were identified from the isolates(Mugoyelaet al.,2010) .Similarly, human normal flora and airborne organisms (such as molds including *Aspergillus*spp., *Penicillium* spp., *Fusarium* spp. and Acremoniumspp) have been reported. (Najmuddin et al.,2010 ; Rauf et al.,2018 ;Gad et al.,2011) . This indicates irregularities during manufacturing, packaging and repackaging. Although not exhaustive, the most common hazardous microorganisms found in pharma-ceutical products and premisesAs a limitation, these results cannot ascertain whether 100% contamination occurred at the production stage because product samples were not directly collected from manufacturing sites. There are chances of microbes getting in if the products are not handled well along the distribution channel, particularly if the supply chain is long. In a measure to mitigate this limitation, samples were obtained from reputable suppliers with well-established distribution channels. For imported products, samples were procured from marketing authorization holders (MAH), while local products were obtained from primary distribution points. In addition, samples were subjected to physical inspections before they were procured.Pharmaceuticals are medicinal products used in the prevention, treatment, and diagnosis of diseases. Therefore, the presence of mycotoxins, especially microorganisms, can reduce or eliminate the therapeutic activity of the product and pose a potential risk to patient health. The presence of microorganisms in oral fluid samples may explain the complexities of treating

infected children. Therefore, a microbiological quality of these drugs is suggested] (Mugoyelaand Mwambete., 2010) . And Medicinal products are not only taken by healthy individuals in good condition but also by sick patients, often with chronic ailments and weakened immune systems. These products must demonstrate therapeutic effectiveness and maintain high quality to ensure the safety of those who use them.Two critical aspects of improper microbiological quality in drugs serve as key parameters in evaluating product quality. These issues may lead to changes in the physicochemical properties of the product, potentially affecting its shelf-life and, in certain cases, causing harm or even life-threatening risks. Microbiological contamination of drugs (Dao et al., 2018 ; Obuekwe and Eichie., 2006) .and Medicinal products available on the market should be characterized by therapeutic efficacy, high quality, and safety for patients. They must either be sterile or comply with the appropriate pharmacopoeial microbiological purity requirements. Pharmacopoeial monographs related to microbiological tests of drug quality were also referenced. Despite stringent regulations governing pharmaceutical production, irregularities in the microbiological quality of drugs still occur. These are monitored by relevant agencies, which may order the recall of defective product batches from the market. However, in recent years, numerous cases of microbiological contamination in drugs and drug-related infections have been reported. Both isolated incidents and larger outbreaks or epidemics linked to contaminated medicines have been documented. Various microorganisms, yeast-like and mould fungi, have been identified in medicinal products or in patients affected by contaminated drugs. Ensuring the appropriate purity or sterility of pharmaceutical raw materials; maintaining cleanliness in the manufacturing environment, facilities, and equipment; and adhering to hygiene protocols and Good Manufacturing Practice regulations are essential for the production of safe and high-quality medicinal products. The aim of this study is to collect and compile information on the microbiological quality of drugs available on the market, with particular attention to identified irregularities, objectionable microorganisms isolated from medicinal products, and drug-related infections (Tyskim et al.,2025).A reduction in patient safety. This includes drug-related infections caused by the presence of live pathogenic microorganisms in medicinal products and medical devices used for drug administration. When a contaminated drug is

administered, microorganisms can grow, multiply, and release toxic substances in the patient's body. Drug poisoning, on the other hand, is caused by cellular and extracellular factors—primarily toxins and enzymes—produced by microorganisms that were present in the raw materials and the finished product. In such cases, live microbial cells may no longer be present, so an infection does not occur (Eissa., 2016; Ahmed et al.,2024 ; Vijayakumar et al., 2012) . Some species of mold are capable of producing toxins, called mycotoxins that can be harmful to humans. These mycotoxins can be some of the most toxic substances in existence. There are several different types of mycotoxins. The types include e.g Aflatoxins, which are produced by *Aspergillus* and include Aflatoxin B1, B2, G1, G2, M1 and M2. (Anonymous) ., 2015; Hubka and Moldenhauer, 2015). The World Health Organization (WHO) has issued numerous guidelines relative to pharmaceutical products as well as to other aspects of life, including those on indoor air quality (WHO, 2000; 2009). For indoor air quality, the guidance indicates many health risks associated with exposure to molds and provides clinical evidence of health exposure to molds. In most cases, remediation of the product may not be possible unless your regulatory submission provides for some type of product reprocessing. Key considerations in responding to the contamination include a root cause analysis of where the contamination came from, corrective actions to eliminate the source of contamination, and preventative actions to prevent recurrence. After that, the issues arise in determining whether the product is safe for use or should be rejected. A product impact analysis should be conducted, keeping in mind the various health risks associated with mold as well as Good Manufacturing Practice (GMP) and quality requirements (Hubka and Moldenhauer., 2015). In 2013, 55 people died from fungal meningitis caused by contaminated steroid injections containing methylprednisolone acetate. Additionally, in 2021, *Aspergillus penicillioides* contamination was reported in ChloraPrep drugs, which was attributed to the storage conditions that were conducive to the growth of this fungus. These incidents have resulted in severe infectious diseases, such as invasive mycoses, cornea infections, Endophthalmitis, and intestinal and gastric mycosis. By implementing preventive measures and policies, it is possible to avoid these outbreaks. Creating Nano-diagnostics presents a major challenge, where promptly diagnosing fungal infections is required to determine the proper corrective and

preventive measures(El-Sayed et al.,2023). However, hypothesized that the patient injected fungus while using illicit drugs, which then seeded the meninges, a strategy described earlier for *Cryptococcal meningitis* caused by *Cryptococcus* and cerebral mucormycosis by *Rhizopus arrhizus* (*Shah et al., 2018; Hopkins et al ., 1994)* .Typically, more than fifty per cent of patients who develop fungal meningitis die(*Gottfredsson and Perfect .,2000)* . A 52% fatality rate for *Aspergillus meningitis* was documented, partly attributable to a high proportion of immune suppressed individuals with disseminated fungal infection(*Kourkoumpetis et al., 2012). The results of this study showed that* agree with the study conducted by (FDA.,2012$_a$) In found of fungus in *Penicillium* sp and *Cladosporium* sp ,*Aspergillus tubingensis* and A.*fumigatus* at drug **Betamethasone** . and study (*Rockoff*.,2013) to found *Alternaria alternate* in drug Risperda consta (Rispseridone) .and with (*FDA., 2021*$_b$) to found Yeast and Mold in Ruzurgi(amifampridine).

Conclusion and Recommendations

Conclusions

All products studied werecontaminated with microorganisms, with most of the products exceeding the maximum acceptable counts were more contaminated than tablets and capsules. Major contaminants were identified to be fungal such as *Aspergillus*spp ,*Alternaria*sp ,*Penicillium*sp ,*Stemphylium*sp and *Candidaparaposilosis*,Fungi are also Known to produce toxins which can be carcinogenic in nature, as such their presencein any pediatrics drug should not be taken lightly, usually most patients are potentially immune compromised when they are taking drugs which accelerate the chances of diseases acquired by opportunistic pathogens, Therefore, the presence of any microorganism should in Libya pharmaceuticals should strictly deal with microbial stringency within the manufacturing which should include packaging, distribution and storage of pharmaceutical products, added preservatives, sweeteners, and production environment. Furthermore,microbial loads of non-sterile pharmaceuticals can be reduced to barest minimum by preventing the possibility of spoilage organisms and by adding well-researched antimicrobial agents orchemicalpreservatives,unhygienic environmental condition coupled with

improperhandling of raw materials, ingredients and products must also be checked finally, good manufacturing practice is non-negotiable and must be strictly adhere to at all times if the microbial contamination is to be totally eradicated (Gad.,2011).Expired drugs, including gastrointestinal medications, are particularly vulnerable to microbial contamination due to potential degradation of preservatives and changes in storage conditions. Studies have shown that expired drugs can harbor a variety of microorganisms, including *Aspergillus niger*, which can pose significant health risks to consumers. The presence of these contaminants in expired drugs underscores the need for stringent quality control measures and proper storage practices to ensure the safety and efficacy of pharmaceutical products.One of the most important sources of fungal contamination is:Pharmacies where drugs are prepared: Fungal outbreaks have been linked to prepared medications, such as contaminated steroid injections that cause fungal meningitis [3Common medications: Studies have identified fungal contaminants such as *Aspergillus niger and Rhizopusstolonifer* in various medications, including Troycaine and Methdilazineand Environmental factors: Fungi such as Fusarium and Exserohilum can survive in adverse conditions, contributing to sporadic contamination(Ahearn and Doyle.,2014)and .Health risks: The presence of fungi in medications increases the risk of drug-resistant infections and allergic reactions, necessitating strict quality control measures and .Quality control: Strict microbial quality control during manufacturing and storage is essential to reduce the risk of contamination and .Rapid detection is essential: The use of nanodiagnostics can enhance the speed and accuracy of fungal detection in medications(Ahmed et al.,2024.

Recommendations

*Avoid the importation of pharmaceuticals from unverified or unknown manufacturers to ensure drug safety and quality.

*Implement international-level surveillance and testing of medications available in both public and private pharmacies across Libya. This includes monitoring the sources, analysing the contents, and verifying the quality of imported and distributed drugs.

*Recognize that expired medications may pose a significant risk of fungal contamination, making their safe disposal essential. Furthermore, the

manufacturing process, packaging, and storage conditions of these drugs play a critical role in preventing such contamination.

*Conduct thorough analysis of active pharmaceutical ingredients (APIs) to verify their identity and composition, ensuring they match the information provided on the packaging and labelling.

*Cease the importation of drugs from certain Egyptian and Indian pharmaceutical companies—specifically *Himalaya* (Egyptian) and *Shifa-Ron* (Indian)—due to documented cases of fungal contamination in their productsSuch contamination poses serious health risks, particularly for the elderly and individuals with chronic illnesses.

*. It is recommended that future researchers investigate bacterial contamination in both expired and unexpired medications, as well as explore fungal contamination in other classes of pharmaceutical products beyond gastrointestinal drugs.

*. Pharmaceutical manufacturers should follow good manufacturing, distribution, and storage practices to avoid contamination and cross-contamination of their products. Relevant medicine regulatory authorities should regularly inspect the manufacturing facilities and conduct post-marketing surveillance (PMS) of the registered products to assess conformity to GMP guidelines. Future studies should involve samples collected directly from manufacturing sites and further extend to assessing the impact of microbial contamination on pharmaceutical products, including medicine-related infections

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