



## Mycotic Quality and Potential Health Implications of Selected Pharmaceutical Syrup Sold in Minna, Niger State, Nigeria

<sup>1</sup>Abah D. O., <sup>1</sup>Bala J. D., <sup>2</sup>Garba D. E., <sup>3</sup>Jesse I. A., <sup>4</sup>Sadiku J. O., <sup>5</sup>Ikegima E. and <sup>\*1,4</sup>Attah F.

Received: October 13, 2024 / Accepted: December 17, 2024

© REJOST 2024

### Abstract

Syrups are liquid medications that contain active ingredients and are ideal for babies, children, and the elderly due to their ease of use. However, their high sugar content and other additives used to enhance taste and stability in syrups make them especially susceptible to microbial growth. This study is aimed at evaluating the mycotic quality of four types of syrup - Vitamin C, Paracetamol, Cough, and Multivitamins sourced from three pharmaceutical stores through spread plate methods. Fungal counts in the samples ranged from  $1 \times 10^1$  to  $4 \times 10^1$  CFU/mL. Mycological analysis identified fungal species including *Aspergillus niger*, *Trichophyton megninii*, *Penicillium notatum*, *Aspergillus fumigatus*, and *Mucorpusillus*, with *Aspergillus niger* and *Trichophyton megninii* being the most frequently detected followed by *mucorpusillus* and *Penicilium notatum*. The mycotic load met the European Pharmacopoeia's fungal limit of  $\leq 10^1$  CFU/mL. The results emphasize the importance of rigorous quality control in pharmaceutical production and storage to prevent microbial contamination and protect patient health. Therefore, it is imperative to promote public awareness campaigns regarding the proper storage of pharmaceutical syrups.

✉ Attah F: [attahf@custech.edu.ng](mailto:attahf@custech.edu.ng) (+2348075425472)

<sup>1</sup>Department of Microbiology, Federal University of Technology, Minna, Niger State, Nigeria

<sup>2</sup>Department of Microbiology, Prince Abubakar Audu University, Anyigba, Kogi State

<sup>3</sup>Department of Biological sciences, Faculty of Science, Taraba State University, Jalingo, Nigeria

<sup>4</sup>Department of Microbiology, Confluence University of Science and Technology, Osara, Kogi State, Nigeria

<sup>5</sup>Bayelsa State Institute of Entrepreneurship and Vocational Training, Elebele, Bayelsa State, Nigeria

**Keywords:** Mycotic quality, Syrup, Contamination, Fungal Load, Fungi

## 1.0 Introduction

Syrups are non-sterile liquid dosage forms containing active medicinal ingredients, making them a highly convenient option for babies, children, and the elderly (Gurung and Rai, 2021). They are primarily designed for oral administration in children, as tablets and capsules are often unsuitable or difficult for them to consume (Martir *et al.*, 2017; Meyers, 2024).

Fungal contamination of syrups is a significant concern in the pharmaceutical industry, particularly for oral liquid medications (Oyebanji *et al.*, 2018). Fungi, such as molds and yeasts, can proliferate in syrup formulations, where the presence of water and sugar creates a favorable environment for their growth. This contamination is problematic because it not only poses potential health risks to consumers, especially children and elderly patients with compromised immune systems, but it can also compromise the quality, stability, and efficacy of the syrup (Haji *et al.*, 2022).

Several factors contribute to fungal contamination in syrups, including poor quality control in raw materials, inadequate sterilization of manufacturing equipment, suboptimal environmental conditions, and improper handling and storage. Fungi such as *Aspergillus*, *Candida*, and *Penicillium* have been commonly identified as contaminants in syrups. These organisms can enter the production process at various stages, from raw material procurement to manufacturing, packaging, and distribution (Sandle, 2016).

Fungal contamination can lead to changes in the physical, chemical, and organoleptic properties of syrups, potentially degrading active ingredients or producing mycotoxins that are harmful to human health (Denyer *et al.*, 2011). Additionally, fungi may cause visible changes in the product, such as discoloration, off-odors, and turbidity, which can indicate spoilage and

reduce patient compliance. In response to these risks, regulatory bodies such as the European Pharmacopoeia Commission and the United States Pharmacopeia have established microbial limits to ensure product safety and quality. However, cases of fungal contamination beyond these limits are still reported globally (Almuzaini and Choonara, 2013).

Preservatives are commonly used in syrups to inhibit microbial growth, including fungi. However, preservative efficacy can vary, and certain strains of fungi may develop resistance, highlighting the need for stringent quality control measures in the pharmaceutical industry (Russell, 2003). Ensuring good manufacturing practices, maintaining clean production environments, and conducting regular microbiological testing are essential steps to minimize fungal contamination and ensure the safety and efficacy of syrup products.

The administration of contaminated syrups poses a significant risk, even with low levels of contamination, as these individuals often have underdeveloped or weakened immune systems, making them more vulnerable to infections (Imarenezor *et al.*, 2021; Gurung and Rai, 2021).

Some of these syrups, such as cough syrups and multivitamin syrups are readily accessible, which raises questions regarding possible variations in microbiological purity across different brands (Gurung and Rai, 2021). Variability may result from variations in quality control procedures, storage settings, or production methods. Thus, it is essential to carry out precise research in order to assess the mycotic quality of the selected syrups sold in Minna, Niger State, Nigeria. These investigations reduce the dangers of microbiological contamination in pharmaceutical syrups and assist in guaranteeing adherence to safety regulations.

## 2.0 Materials and methods

### 2.1 Sample collection

Four selected syrups (Vitamin C, Paracetamol, Cough, and Multivitamin) were purchased from registered pharmaceutical stores located in Maitumbi, Mobil, and Tunga, making a total of 12 samples. Each syrup sample had a unique batch number, NAFDAC registration status, manufacturing date, and expiry date. The selected syrups samples purchased from

registered pharmaceutical stores were transported to Microbiology laboratory in the Department of Microbiology, Federal University of Technology Minna for further mycotic analysis. The syrup samples were properly labelled. Syrup sample purchased from Maitumbi were labelled as CSMB, PSMB, MVMB and VCMB; Mobil (CSML, PSML, MVML and VCML) and Tunga (CSTA, PSTA, MVTA and VCTA).

**Table 1:** The details of syrups sample collection

| Location | Company Code | Sample Code | Manufacturing Date | Expiring Date | Batch Number | NAFDAC Number |
|----------|--------------|-------------|--------------------|---------------|--------------|---------------|
| Maitumbi | A            | CSMB,       | 12/2018            | 11/2020       | TCC162       | 04-3494       |
|          |              | PSMB        | 04/2019            | 04/2021       | PMS 22       | 04-3414       |
|          |              | MVMB        | 04/2019            | 04/2021       | DVS 5        | 04-2954       |
|          |              | VCMB        | 06/2019            | 06/2021       | VCS 88       | 04-2907       |
| Mobil    | B            | CSML,       | 07/2019            | 06/2022       | SS1917       | A4-7989       |
|          |              | PSML,       | 10/2016            | 09/2019       | PS 1645      | A4-7990       |
|          |              | MCML        | 06/2019            | 05/2021       | MV1904       | A11-0082      |
|          |              | VCML        | 07/2019            | 06/2021       | VS1916       | A4-7988       |
| Tunga    | C            | CSTA        | 03/2019            | 02/2021       | A0279        | A4-0206       |
|          |              | PSTA,       | 06/2019            | 06/2021       | A0125        | 04-8288       |
|          |              | MVTA        | 02/2019            | 07/2020       | A061         | B4-1398       |
|          |              | VCTA        | 07/2019            | 02/2021       | A0149        | 04-5585       |

**KEY:** CSMB = Cough Syrup Maitumbi, CSML= Cough Syrup Mobil, CSTA= Cough Syrup Tunga.

### 2.2 Total Mold and Yeast Count (TYMC)

The mold and yeast counts were determined by spread plate methods. One milliliter from each sample was withdrawn aseptically and transferred into 9 ml normal saline for serial dilution to  $10^2$ . Diluted samples were thoroughly mixed for proper dissolution of the drug. 0.1ml of each sample from  $10^1$  was spread onto potato dextrose agar. The plates were incubated at 25°C for 3-5 days, after which fungal colonies were counted using a colony counter. The average colony-forming units (CFU) per millilitre of syrup sample were then calculated.

### 2.3 Isolation and identification of fungal isolates

The fungal isolates were identified using their cultural and morphological characteristics as

outlined by Harold (2002). A drop of lactophenol cotton blue stain was dropped in the centre of a clean grease free slide and then a fragment of the fungus was collected with the aid of a sterile inoculating needle and placed in the drop of the stain and teased gently and covered with a cover slip. The slide was examined under the microscope, first with (x10) and then with (x40) objective lens for its morphological characteristics (Cheesbrough, 2006). The isolates were identified by comparing their characteristics with those of known taxa using the schemes of Domsch and Gams (1970).

### 2.4 Data Analysis

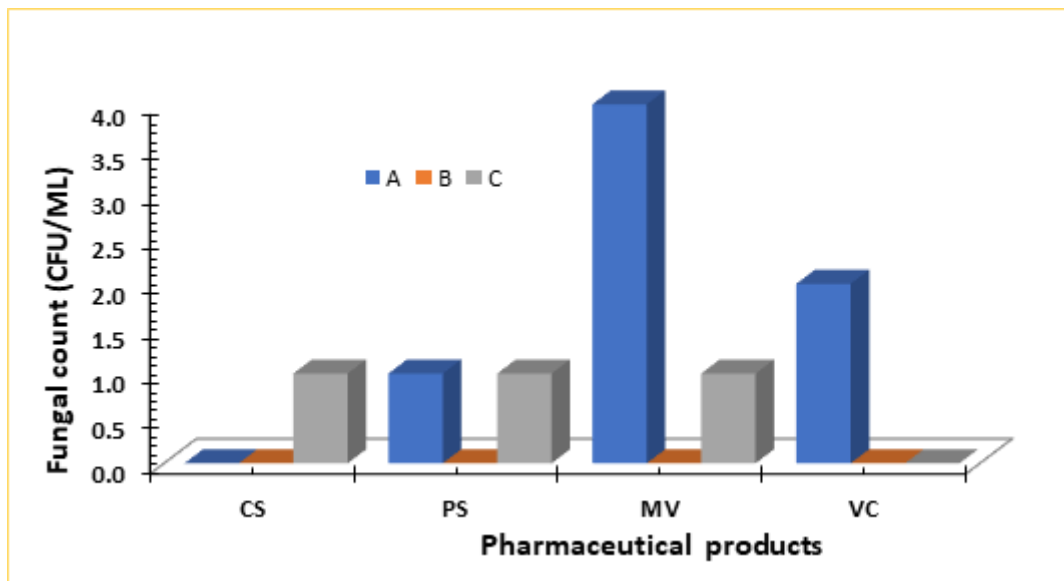
Data obtained from the study was tabulated as Microsoft Excel sheet and statistical analysis was performed.

### 3.0 Results

#### 3.1 Results of total fungal load in syrup purchased from a registered pharmaceutical store

Figure 1 presents the results of the total fungal load in syrup samples purchased from registered pharmaceutical stores in Maitumbi (A), Mobil (B), and Tunga (C). The analysis revealed that cough syrup (CS) from locations A and B

showed no fungal growth, while vitamin C (VC) from location C also exhibited no growth. Among the samples, multivitamin (MV) from location A had the highest fungal load, followed by vitamin C (VC) from the same location. In contrast, samples of paracetamol syrup (PS), MV, and VC from location B showed no detectable fungal growth.



**Figure 1:** Total fungal count in syrups purchased from registered pharmaceutical stores located at Maitumbi, Mobil and Tunga

#### 3.2 Cultural and Morphological Characteristics of Fungi Isolates

The cultural and morphological characteristics of the fungi isolated revealed the followings: *Aspergillus niger*, *Aspergillus fumigatus*, *Penicillium notatum*, *Trichophyton megninii* and *Mucorpusillus* based on the appearance and texture types of spores, hyphae and rhizoid as shown in Table 3.

#### 4.0 Discussion

The findings of this investigation into fungal contamination in syrup samples from various locations highlight significant concerns about the microbial safety of pharmaceutical syrups (Halls, 2016). The fungal load in four syrup samples from three different locations ranged

from  $1 \times 10^1$  to  $4 \times 10^1$  CFU/ml. The absence of fungal growth in samples from location B could be attributed to good storage conditions, as the same products from other locations were found to be contaminated. Jazmati *et al.* (2022) reported similar results in their investigation of 29 different syrups in Syrian pharmacies.

The results of this study do not exceed the total fungal limit recommended by the European Pharmacopoeia (EP, 2010), as cited by Ratajczak *et al.* (2015). Jameel (2017) also reported instances of fungal contamination in some syrup. Such contamination may occur during the manufacturing, processing, marketing, or administration of pharmaceutical products (Lebelo *et al.*, 2021).

**Table 3:** Cultural and Morphological Characteristics of Fungi Isolates

| Isolate code | Appearance on media                | Texture on media | Types of spore                     | Type of Hyphae | Rhizoid | Fungi Name                   |
|--------------|------------------------------------|------------------|------------------------------------|----------------|---------|------------------------------|
| CSTA         | Black with fluffy appearance       | Rough            | Conidiophore                       | Septate hyphae | Present | <i>Aspergillus niger</i>     |
| CSTA         | Blue-green appearance              | Rough            | Conidiophore                       | Septate hyphae | Present | <i>Penicillium notatum</i>   |
| VCMB         | Black with fluffy appearance       | Rough            | Conidiophore                       | Septate hyphae | Present | <i>Aspergillus niger</i>     |
| PSTA         | Pink, velvety, spoke- like grooves | Rough            | Roundish, oval, pear-shape conidia | Septate hyphae | Absent  | <i>Trichophyton megninii</i> |
| PSMB         | Pink, velvety, spoke- like grooves | Rough            | Roundish, oval, pear-shape conidia | Septate hyphae | Absent  | <i>Trichophyton megninii</i> |
| MVMB         | Grey-green                         | Rough            | Conidiophore                       | Non-septate    | Absent  | <i>Aspergillus fumigatus</i> |
| MVTA         | White                              | Smooth           | Sporangiophore                     | Non-septate    | Present | <i>Mucorpusillus</i>         |

**KEY:** CSMB= Cough Syrup Maitumbi, CSML= Cough Syrup Mobil, CSTA= Cough Syrup Tunga.

The present of *Aspergillus niger*, a well-known environmental pollutant that grows well in a variety of substrates, particularly in warm, humid environments. Additionally, it is known to produce mycotoxins, which can be detrimental to human health, particularly for those with weakened immune systems (Denning *et al.*, 2015). In rare instances, *A. niger* can cause respiratory infections and other invasive diseases, and consuming items tainted with its mycotoxins may have hazardous effects (Awuchi *et al.*, 2022). This is especially troubling when it comes to drugs meant for groups who may be more sensitive to this danger, such as youngsters or the elderly (Gao *et al.*, 2022).

*Penicillium notatum*, on the other hand, while generally considered less pathogenic, can still pose risks in pharmaceutical products (Frasz and Miller, 2015). This fungus can contribute to product spoilage, impacting both the taste and therapeutic efficacy of the syrup (Iacumin *et al.*, 2022). Spoilage caused by fungal growth may

degrade active ingredients, potentially lowering the effectiveness of the medication (Kamil and Lupuliasa, 2011). The presence of *P. notatum* indicates possible issues in quality control during manufacturing or storage, as even minor deviations in environmental conditions or hygiene standards can lead to contamination by this resilient genus (Frisvad *et al.*, 2004). Though *P. notatum* itself is not often directly harmful, the contamination suggests lapses in sanitation protocols or storage issues that could also allow more dangerous fungi to proliferate.

The identification of *Trichophyton megninii* in a syrup sample is notable, as this fungus is typically associated with dermatophyte infections, affecting skin, nails, and hair in humans (Enurah *et al.*, 2020). Although its presence in pharmaceutical syrups suggests contamination from handling procedures, environmental exposure, or cross-contamination from non-sterile equipment, it is less frequently discovered in consumables (Gupta *et al.*, 2001). This kind of contamination implies that there

may be additional; less evident contaminants present and indicate violations in the hygienic standards of the production or packing procedures.

Finally, *Mucorpusillus* and *Aspergillus fumigatus* in syrup samples could indicate significant fungal contamination, especially considering the pathogenic nature of these organisms. *Aspergillus fumigatus* is known to cause respiratory issues and can be particularly dangerous for immune - compromised individuals, while *Mucorpusillus* is associated with spoilage and potential mycotoxin production (Dinev *et al.*, 2023).

There are several possible origins of fungal infection in syrups. The use of raw materials that were not sufficiently screened or sterilized, manufacturing errors, inadequate sanitation procedures, or storage circumstances that encourage the growth of fungi are examples of potential contamination pathways (Russell, 2003). Because syrups frequently contain sugars or other carbohydrates that, if not stored in regulated circumstances, provide fungi with an optimal food foundation, storage conditions are very important in preventing fungal infection.

## 5.0 Conclusion

In conclusion, the findings highlight the potential risks posed by fungal contamination in pharmaceutical syrups, which could have serious health implications, especially for vulnerable populations like children and the elderly. Fungi like *Aspergillus niger*, *Penicillium notatum*, *Trichophyton megninii*, *Mucorpusillus*, and *Aspergillus fumigatus* were found in syrup samples, which suggests that there were problems with storage and quality control. These contaminants, particularly those capable of producing mycotoxins or causing respiratory infections, highlight the critical need for stringent hygiene and quality assurance protocols throughout the manufacturing and distribution process.

## Conflict of interest

The authors declared no conflict of interest.

## Acknowledgement

We extend our heartfelt gratitude to Professor J.D. Bala for his invaluable contributions to the success of this research. We also acknowledge Attah F. and Abah D.O. for their intellectual contributions. Additionally, we recognize and appreciate the efforts of the remaining author

## References

- Almuzaini, T., & Choonara, I. (2013). Problems associated with substandard and counterfeit medicines in developing countries. *British Journal of Clinical Pharmacology*, 75(3), 2013.
- Awuchi, C. G., Ondari, E. N., Nwozo, S., Odongo, G. A., Eseoghene, I. J., Twinomuhwezi, H., & Okpala, C. O. R. (2022). Mycotoxins' toxicological mechanisms involving humans, livestock and their associated health concerns: A review. *Toxins*, 14(3), 167.
- Cheesbrough, M. (2006). *District Laboratory Practice in Tropical Countries*. Cambridge University Press.
- Denning, D. W., Pleuvry, A., & Cole, D. C. (2015). Global burden of chronic pulmonary aspergillosis as a sequel to pulmonary tuberculosis. *Bulletin of the World Health Organization*, 89, 864–872.
- Denyer, S. P., Hodges, N. A., & Gorman, S. P. (2011). *Hugo and Russell's Pharmaceutical Microbiology*. John Wiley & Sons.

- Dinev, T., Velichkova, K., Stoyanova, A., & Sirakov, I. (2023). Microbial Pathogens in Aquaponics Potentially Hazardous for Human Health. *Microorganisms*, 11(12), 2824.
- Domsch, K. H., Gams, W. (1970). Fungi in agricultural soils, Longman Group Limited, London, pp. 20-152.
- Frasz, S. L., & Miller, J. D. (2015). Fungi in Ontario maple syrup & some factors that determine the presence of mold damage. *International journal of food microbiology*, 207, 66-70.
- Frisvad, J. C., Frank, J. M., Houbraken, J. A. M. P., Kuijpers, A. F. A., & Samson, R. A. (2004). New ochratoxin A producing species of *Aspergillus* section Circumdati. *Studies in Mycology*, 50, 23–43.
- Gao, Y., Qu, M., Song, C., Yin, L., & Zhang, M. (2022). Cerebral vasculitis caused by *Talaromyces marneffeii* and *Aspergillus niger* in a HIV-positive patient: A case report and literature review. *Journal of Neuro Virology*, 1-7
- Gurung, K., & Rai, M. K. (2021). Assessment of Microbial qualities of some cough syrups and multivitamins marketed in Pokhara, Nepal. *Prithvi Academic Journal*, 4, 1-6.
- Gupta, A. K., Summerbell, R. C., & Cooper, E. A. (2001). Mycology in dermatology. *Journal of the American Academy of Dermatology*, 45(5), 764–788.
- Haji, M., Kerbache, L., & Al-Ansari, T. (2022). Food quality, drug safety, and increasing public health measures in supply chain management. *Processes*, 10(9), 1715.
- Halls, N. (2016). Contamination of Aqueous-Based Nonsterile Pharmaceuticals. In *Microbiological Contamination Control in Pharmaceutical Clean Rooms* (pp. 97-126). CRC Press.
- Harold, B. (2002). *Microbial Application, Laboratory Manual*. 8<sup>th</sup> edition. McGraw-Hill. New York, PP.470-471.
- Iacumin, L., Pellegrini, M., Colautti, A., Orecchia, E., & Comi, G. (2022). Microbial Characterization of Retail Cocoa Powders and Chocolate Bars of Five Brands Sold in Italian Supermarkets. *Foods*, 11(18), 2753.
- Imarenezor, E. P. K., Abhadionmhen, O. A., Shinggu, P. P., Briska, J., George, O. S., & Danya, S. (2021). Bacterial contamination of retailed syrups traded in Wukari, North East, Nigeria. *International Journal of Biological and Pharmaceutical Sciences Archive*, 2021, 02(01), 117–125
- Jameel F. (2017) Microbiological Analysis of Marketed Available Cough Syrups in Karachi. *RADS J. Biol. Res. Appl. Sci* 8(2):5-10.
- Kamil, O. H., & Lupuliasa, D. (2011). Modern aspects regarding the microbial spoilage of pharmaceutical products. *Farmacia*, 59(2), 133-46.
- Jazmati, F. N., Trefi, S., Ibrahim, A., & Bitar, Y. (2022). Microbial evaluation of some syrups in Syrian pharmacies. *Heliyon*, 8(5). 1 – 5.
- Lebelo, K., Malebo, N., Mochane, M. J., & Masinde, M. (2021). Chemical contamination pathways and the food safety implications along the various stages of food production: a

- review. *International journal of environmental research and public health*, 18(11), 5795.
- Martir, J., Flanagan, T., Mann, J., & Fotaki, N. (2017). Recommended strategies for the oral administration of paediatric medicines with food and drinks in the context of their biopharmaceutical properties: a review. *Journal of Pharmacy and Pharmacology*, 69(4), 384-397.
- Meyers, R. S. (2024). The Past, Present, and Future of Oral Dosage Forms for Children. *The Journal of Pediatric Pharmacology and Therapeutics*, 29(1), 22-31.
- Nester, M.T., Anderson, D.G., Robert, C.E. Jr. & Pearsall, N.N. (2002). Microbiology- A Human Perspective. *Genitourinary Infections and Antimicrobial Medications*. 3<sup>rd</sup> ed. Madrid, Spain: MacGraw Hill.
- Oyebanji, E. O., Adekunle, A. A., Coker, H. A. B., & Adebami, G. E. (2018). Mycotic loads' determination of non-sterile pharmaceuticals in Lagos state and 16 rDNA identification of the fungal isolates. *Journal of Applied Pharmaceutical Research*, 6(2), 16-28.
- Ratajczak, M., Kubicka, M. M., Kamińska, D., Sawicka, P., & Długaszewska, J. (2015). Microbiological quality of non-sterile pharmaceutical products. *Saudi Pharmaceutical Journal*, 23(3), 303-307.
- Russell, A. D. (2003). Similarities and differences in the responses of microorganisms to biocides. *Journal of Antimicrobial Chemotherapy*, 52(5), 750-763.
- Sandle, T. (2016). Fungal contamination and infection control in pharmaceuticals. *American Pharmaceutical Review*, 19(1), 56-61.
- WHO. (2010). World Health Organization. *International Pharmacopoeia*, WHO, Technical Report Series, No. 957.