

## ORIGINAL RESEARCH ARTICLE

## Microbiological quality control of non-sterile pediatric pharmaceutical products

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## Abstract

Pharmaceutical pediatric products—whether sterile or non-sterile—must meet the relevant microbiological quality standards to ensure safety and efficacy. During production and use, many pharmaceutical pediatric products are vulnerable to contamination from a wide range of microbial species. Young children under 5 years of age and infants are particularly vulnerable to harmful and accidental infections due to their immature immune systems and limited prior exposure to antigens. When these young children consume pharmaceutical preparations of inadequate microbiological quality, they may be exposed to serious health risks. Maintaining the safety and efficacy of non-sterile pediatric pharmaceutical products, as well as safeguarding children's health, depends on their microbiological quality. Pharmaceutical pediatric products are widely used in India; therefore, it is essential to assess their microbiological quality and overall safety. This study examines the microbiological quality of 26 pediatric drug products. Using compendial methods, the pediatric drug products were analyzed for the presence of specified microorganisms, total yeast and mold count, and total aerobic microbial count. Based on the study's findings, three of the pediatric drug products showed microbial contamination levels above the maximum acceptable limits specified in the Indian Pharmacopoeia. The pediatric drug products under examination did not contain the specified microorganisms, including *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. It is advised that current good manufacturing practices and appropriate hygiene measures be strictly followed when manufacturing, handling, and dispensing these products; therefore, microbial quality control is crucial to prevent contaminated products from reaching the market and to protect public health.

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## 1. Introduction

From a microbiological perspective, pharmaceutical products (PPs) are broadly classified as sterile or non-sterile. Those that contain no viable microorganisms are referred as sterile. Non-sterile products are also manufactured in a controlled

environment; however, they may not be completely free from microorganisms. Therefore, regulatory agencies specify microbiological limits for these products in their finished dosage forms.<sup>1</sup> Pharmaceutical drugs designed for pediatric use must meet stringent quality control requirements to establish their safety and microbiological quality.<sup>2</sup> Infants and children are extremely vulnerable to microbial infection because they have developing immune systems, lower body weight, and greater susceptibility compared with adults.<sup>3</sup> Many pediatric products, such as syrups, suspensions, and chewable tablets, are non-sterile, and these can act as a growth medium for microorganisms if they become contaminated.<sup>4</sup>

Products administered orally or topically are more likely to be contaminated because of inappropriate handling, storage, or contact with contaminated surfaces. The risk of microbial growth increases with time because liquid formulations, such as syrups, are often used repeatedly over weeks or months.<sup>5</sup> Certain oral dosage forms may act as substrates for microbial proliferation if they are stored in conditions conducive to bacterial growth. Particularly in oral liquid medications, moisture and a high sugar content can promote the growth of microorganisms. Pediatric oral liquid formulations, including aqueous solutions, suspensions, emulsions, and syrups, are more susceptible to microbial contamination because of sweeteners, reconstitution techniques, inappropriate handling, and suboptimal storage conditions. In children, microbial contamination PPs may eventually lead to secondary bacterial infections.<sup>5,6</sup>

For pediatric PPs, compendial bodies such as the Indian Pharmacopoeia (IP) and European Pharmacopoeia (EP) recommend rigorous microbiological quality control testing to ensure safety and efficacy. Microbiological purity must be ensured to prevent contamination that can lead to toxicity, infection, or reduced effectiveness of treatment in children. Microbiological purity is a critical quality attribute for the overall safety and quality control of pediatric medicines.<sup>7</sup>

Although most of the pharmacopeias do not require non-sterile preparations to be sterile, such preparations are required to pass the microbial bioburden tests for total

aerobic microbial count (TAMC) and total yeast and mold count (TYMC), and should be devoid of certain specified microorganisms such as *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* to verify their efficacy and safety.<sup>8,9</sup> Pharmaceutical acceptance standards must be rigorously followed in accordance with the approved specifications of the IP or the EP. In this regard, the final products of non-aqueous preparations should have a TAMC of  $<1 \times 10^3$  colony-forming unit (CFU)/g or mL and a TYMC of not more than  $1 \times 10^2$  CFU/g or mL, whereas aqueous preparations and products for cutaneous use should have a TAMC of  $<1 \times 10^2$  CFU/g or mL and a TYMC of not more than  $1 \times 10^1$  CFU/g or mL.<sup>10-12</sup>

PPs may become contaminated by microorganisms at any stage during manufacturing, packaging, and distribution. Contamination may arise from a variety of sources, including workers, equipment, raw materials, and the manufacturing equipments. Bacteria, fungi, viruses, and yeasts are examples of microbiological contaminants. These microorganisms can grow in a variety of environments, including the moist, nutrient-rich conditions found in many PPs. Microorganisms not only shorten a product's shelf life but also pose major safety risks, especially in non-sterile drug products. Even a small number of contaminating microorganisms can cause life-threatening illnesses in pediatric patients with underdeveloped immune systems.<sup>13</sup> India's pharmaceutical industry, ranking among the highest in the world in manufacturing generic drugs, faces a significant challenge in upholding microbiological standards, especially in small- and medium-scale facilities with variable adherence to good manufacturing practices (GMP).<sup>14</sup>

Many pediatric drugs are formulated as non-sterile preparations; therefore, they may contain a variety of microorganisms, including potentially hazardous ones if microbiological controls are inadequate. In such instances, children with a relatively weak immune system may be adversely affected by the use of these medications. As a result, regular microbiological testing of pharmaceutical drug products, particularly oral medications commonly delivered to children, is critical for consumer safety. Table 1 lists the acceptance criteria for the microbiological

**Table 1. Acceptance criteria for the microbiological quality of non-sterile oral preparations, aqueous and non-aqueous dosage forms, and products intended for cutaneous use**

Dosage form/route of administration	TAMC (CFU per g or mL)	TYMC (CFU per g or mL)	Specified microorganism (absent in 1 g or 1 mL)
Aqueous preparation (Oral)	$10^2$	$10^1$	<i>Escherichia coli</i>
Non-aqueous preparation (Oral)	$10^3$	$10^2$	<i>Escherichia coli</i>
Cutaneous use	$10^2$	$10^1$	<i>Staphylococcus aureus</i> , <i>Pseudomonas aeruginosa</i>

Abbreviations: CFU: Colony-forming unit; TAMC: Total aerobic microbial count; TYMC: Total yeast and mold count.

quality of non-sterile oral preparations, aqueous and non-aqueous dosage forms, and cutaneous use. Several studies have evaluated the microbiological quality of non-sterile pediatric drugs in countries such as Spain, Bangladesh, Ghana, and Sri Lanka.<sup>2,5,15,16</sup> To date, no comparable studies have been conducted in India, which limits the ability to adequately assess the safety of commercially available pediatric medicines. Therefore, the current investigation was designed to determine bacterial and fungal counts in non-sterile pediatric products purchased from local markets in Ghaziabad, India, and to assess the presence or absence of specified microorganisms using compendial microbial testing methods described in the IP.<sup>5,9</sup>

## 2. Materials and methods

### 2.1. Collection of pediatric drug products

Pediatric drug products (PDPs) from different manufacturers were collected from both urban and rural areas of the district Ghaziabad, Uttar Pradesh, India. They were readily obtainable from numerous pharmacies. The non-sterile PDPs comprised 25 oral preparations and 1 topical preparation. The oral pediatric preparations included syrups, whereas the topical preparation consisted of a cream.

### 2.2. Physical examination of the pediatric drug products

To determine physical quality and key characteristics, each PDP was examined for appearance, odor, manufacturer label, expiry dates, and brand. The packaging material was also inspected for leaks and cracks.

### 2.3. Workspace

To safeguard the products and testing preparations from environmental contamination, each PDP evaluation was conducted in a controlled environment using a horizontal laminar air flow hood (Toshiba, India). The hood was equipped with a high-efficiency particulate air filter rated at 0.3 µm, providing 99.99% filtration efficiency for airborne particles and microorganisms.

### 2.4. Instruments used

The following instruments were used throughout the study: Autoclave (Natsteel, India), colony counter (Mac, India), biochemical oxygen demand (BOD) incubator (Sonar, Sciencetech, India), laminar air flow hood, pH meter (Mettler Toledo, India), microscope (Olympus, Japan), hot air oven (Tanco, India), and top pan balance (Aczet, India).

### 2.5. Media preparation, growth promotion, and the indicative and inhibitory properties of culture media

Dehydrated media used in the present study were obtained from HiMedia Laboratories Private Limited

(Mumbai, India). The following media were used for microbiological analysis: Sabouraud dextrose agar (SDA) for TYMC, soyabean casein digest medium (SCDM) as a diluent for sample pre-treatment, soyabean casein digest agar (SCDA) for TAMC, MacConkey broth for *E. coli* pre-enrichment, MacConkey agar as an *E. coli* selective medium, mannitol salt agar as a selective medium for *S. aureus*, and cetrimide agar as a selective medium for *P. aeruginosa*. Buffered sodium chloride–peptone solution was prepared by dissolving 1.0 g of the dehydrated sodium chloride–peptone powder in distilled water and adjusting the volume to 1000 mL. 100 mL portions were then transferred into flasks. In accordance with the IP, the prepared media were autoclaved for 20 min at 121°C and 15 psi to achieve sterilization and were then examined for growth promotion, indicative properties, and inhibitory properties.

### 2.6. Negative control

The diluent alone was used as a negative control to confirm the test conditions. No microbial growth was expected to appear in this control, as any growth would indicate compromised test validity.

### 2.7. Preparation of pediatric drug products

Sample preparation was conducted according to the procedure given in the IP. During sample preparation, physical characteristics of the products were recorded as described in the IP. Before opening the samples, the outside surfaces of each package were thoroughly sterilized using 70% v/v ethanol. A 1:10 dilution of the test sample was generated aseptically using a 10 mL sample of syrup or 10 g of cream in 90 mL sterilized SCDM, as described in the general chapter “Microbial Contamination in Non-Sterile Products” of the IP 2022. The material was serially diluted using the same diluent and was used to enumerate TAMC and TYMC.

### 2.8. Microbial enumeration test

Two well-established techniques—the pour-plate technique and the membrane filtration method—were employed to enumerate microorganisms in PDPs, in accordance with the IP 2022. The method was selected based on the type of PP under study. Total TAMC and TYMC in non-antibiotic syrup samples were measured using the pour-plate method.

#### 2.8.1. Pour plate method

A total of 1 mL of the diluted sample (1:10 dilution, and further dilutions if required) was aseptically transferred into two sterilized 90-mm-diameter Petri plates. For TAMC, 20 mL of SCDA (cooled to approximately 45°C) was added to each of the two Petri plates, and for TYMC,

20 mL of sterile SDA (cooled to approximately 45°C) was added to the other two Petri plates. The contents of each Petri plate were mixed by gently rotating the plate to ensure that the sample and medium were well mixed, and the mixture was then left to solidify.

For TAMC, the solidified SCDA plates were incubated in a BOD incubator at 30–35°C for 3–5 days, whereas the SDA plates were inverted and incubated at 20–25°C for 5–7 days. Petri plates with CFU counts <250 for TAMC and <50 for TYMC were selected after the incubation period. By choosing the appropriate dilution, the mean CFU/g or mL of material was determined.<sup>17</sup>

### 2.8.2. Membrane filtration

The membrane filtration method was selected for antibiotic-containing oral liquid formulations, such as suspensions containing antimicrobial drugs, because the presence of antimicrobial agents may interfere with microbial growth when tested using the traditional pour-plate technique. A 0.45-µm pore-size membrane filter was inserted into a filter funnel that was attached to a vacuum flask. The membrane filter was aseptically loaded with 1 mL of the diluted sample. Immediately afterward, the fluid was vacuum-filtered through the membrane. Each membrane was then rinsed with pH 7.0 buffered sodium chloride–peptone solution to remove residual components. The membrane filter was then transferred onto the surface of 20 mL solidified SCDA plates, and the plates were incubated at 30–35°C for 3–5 days to determine TAMC. For TYMC, the same procedure was followed, using 20 mL solidified SDA plates and incubation at 20–25°C. To determine the number of microorganisms per g or mL of product, the colonies on each plate were counted after incubation.<sup>18</sup>

## 2.9. Tests for the detection of specified microorganisms in aqueous drug products

The aqueous drug products were tested for *E. coli* in accordance with the procedure established by the IP 2022.

### 2.9.1. *E. coli*

For the detection of *E. coli*, samples were prepared as described in Section 2.7. SCDM (90 mL) was inoculated with 10 mL (equivalent to 1 g or 1 mL) of pre-treated sample, and the mixture was incubated for 18–24 h at 30–35°C. Following incubation, 1 mL of SCDM was transferred to 50 mL of MacConkey broth, the mixture was shaken to ensure proper mixing, and then incubated for 24–28 h at 40–42°C. After incubation, the tube was shaken, and a loopful of MacConkey broth was streaked onto a plate of MacConkey agar using a sterile inoculation loop. For 18–72 h, the MacConkey agar plates were then inverted and incubated at 30–35°C. The growth of non-mucoid,

pink colonies on the MacConkey agar plates indicates the presence of *E. coli*.

## 2.10. Test for the detection of specified microorganisms in cutaneous drug products

The cutaneous drug products were tested for *S. aureus* and *P. aeruginosa* in accordance with the procedure established in the IP 2022.

### 2.10.1. *S. aureus*

For the detection of *S. aureus*, samples were prepared as described in Section 2.7. SCDM (90 mL) was inoculated with 10 mL (equivalent to 1 g or 1 mL) of pre-treated sample and incubated for 18–24 h at 30–35°C. Following incubation, the broth was shaken, and a loopful was streaked on a plate of mannitol salt agar using a sterile inoculating loop. The plates were then inverted and incubated at 30–35°C for 18–72 h, and the growth of yellow or white colonies encircled by a yellow zone indicates the potential presence of *S. aureus*.

### 2.10.2. *P. aeruginosa*

For the detection of *P. aeruginosa*, samples were prepared as described in Section 2.7. SCDM (90 mL) was inoculated with 10 mL (equivalent to 1 g or 1 mL) of pre-treated sample, and the mixture was incubated for 18–24 h at 30–35°C. Following incubation, a loopful of the broth was streaked on a cetrimide agar plate using a sterile inoculating loop after it had been shaken. The cetrimide agar plates were then inverted and incubated for 18–72 h at 30–35°C. The development of greenish colonies on cetrimide agar plates indicates the presence of *P. aeruginosa*.

## 3. Results

### 3.1. Evaluation of microbiological quality

A total of 26 distinct non-sterile pharmaceutical pediatric products were analyzed for microbial contamination. Each product was labeled with the manufacturer's name and expiry dates. Physical inspection revealed no changes in appearance, leakage, or cracks, and the packaging did not show evidence of tampering. As shown in Table 2, of the 26 PDPs examined, three products (one antihistamine, one antispasmodic, and one antipyretic) showed microbial growth, indicating microbial contamination.

Microbiological quality evaluation of aqueous PDPs was conducted in terms of TAMC, TYMC, and the absence of *E. coli*. As illustrated in Figure 1, of the 25 aqueous PDPs evaluated, 22 met the acceptable limits for TAMC, whereas 3 exceeded the standard limit and did not comply. For TYMC, 24 aqueous PDPs were found to meet the standard limit, with 1 exceeding the standard limit and thus not

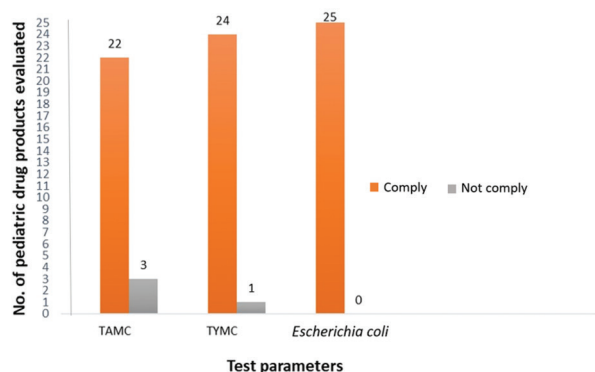


complying with acceptable limits. In the determination of the presence of *E. coli*, none of the 25 PDPs were contaminated, thereby complying with the specified limits. The findings showed that most of the products tested conformed to microbiological quality standards, with only minor variations in TAMC and TYMC.

In addition, the microbiological analysis of the cutaneous PDP was conducted for TAMC, TYMC, and the absence of *P. aeruginosa* and *S. aureus*. As depicted in Figure 2, the cutaneous PDP tested met the acceptable limits for TAMC and TYMC and hence complied with the specified limits. In the tests for *S. aureus* and *P. aeruginosa*, the cutaneous PDP showed no contamination and therefore met the acceptance criteria. These results indicate that the cutaneous PDP complied with the expected microbiological quality standards.

**Table 2. List of pediatric drug products from different categories and subcategories**

Category	Subcategory	Total products tested	No. of contaminated products
Aqueous	Antihistamine	6	1
	Antacid	1	0
	Antipyretic	9	1
	Antibiotic	2	0
	Supplement	2	0
	Antispasmodic	1	1
	Antiemetic	2	0
	Expectorant	2	0
Cutaneous	Cream	1	0
Total	-	26	3



**Figure 1.** Compliance and non-compliance status of aqueous pediatric drug products evaluated for TAMC, TYMC, and *Escherichia coli* in Ghaziabad, India

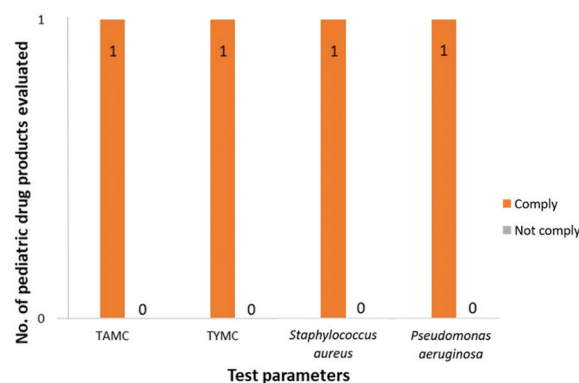
Abbreviations: TAMC: Total aerobic microbial count; TYMC: Total yeast and mold count.

### 3.2. TAMC, TYMC, and specified microorganisms

The microbiological quality of 25 aqueous PDPs was assessed for TAMC, TYMC, and the presence of *E. coli* (Table 3). Of the 25 aqueous PDPs tested, 22 were found to comply with the IP and EP limits for TAMC ( $<1 \times 10^2$  CFU/mL) in the majority of pediatric products. Three PDPs (PP 12, PP 18, and PP 22) were found to have elevated TAMC values of  $1.6 \times 10^2$ ,  $1.51 \times 10^3$ , and  $3.2 \times 10^2$  CFU/mL, respectively; hence, PP 12, PP 18, and PP 22 did not comply with the acceptance criteria of the IP and EP.

In terms of TYMC, compliance was noted in 24 of 25 products, with counts  $<10$  CFU/mL, except for one (PP 18), which had  $8.3 \times 10^2$  CFU/mL, exceeding the acceptable limit. Because *E. coli* was absent from all tested aqueous PDPs, these products achieved 100% compliance with this critical safety requirement. Overall, the majority of the aqueous PDPs complied with the microbiological quality criteria of the IP and EP, with only one product (PP 18) failing in both TAMC and TYMC, and two PDPs (PP 12 and PP 22) failing in TAMC. These results reflect generally acceptable microbiological quality, indicative of good hygiene and manufacturing practices, with some isolated instances of contamination that require corrective action.

The microbiological quality of cutaneous PDP (PP 1) was assessed for TAMC, TYMC, and the presence of *S. aureus* and *P. aeruginosa* (Table 4). The findings revealed that the product complied with the IP and EP acceptance criteria for TAMC and TYMC ( $<1 \times 10^2$  CFU/mL). In addition, *S. aureus* and *P. aeruginosa* were absent in the cutaneous PDP, thereby complying with the IP and EP acceptance criteria. These results demonstrated complete microbiological compliance of the cutaneous pediatric preparation and affirmed



**Figure 2.** Compliance and non-compliance status of cutaneous pediatric drug products evaluated for TAMC, TYMC, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* in Ghaziabad, India

Abbreviations: TAMC: Total aerobic microbial count; TYMC: Total yeast and mold count.

**Table 3. Results of TAMC, TYMC, and specified pathogen in aqueous pediatric drug products**

No. of aqueous PPs	TAMC (CFU/mL)	TYMC (CFU/mL)	Absence/presence of <i>Escherichia coli</i> per mL
PP 1	<1×10 <sup>1</sup>	<1×10 <sup>1</sup>	Absent
PP 2	<1×10 <sup>1</sup>	<1×10 <sup>1</sup>	Absent
PP 3	<1×10 <sup>1</sup>	<1×10 <sup>1</sup>	Absent
PP 4	<1×10 <sup>1</sup>	<1×10 <sup>1</sup>	Absent
PP 5	<1×10 <sup>1</sup>	<1×10 <sup>1</sup>	Absent
PP 6	<1×10 <sup>1</sup>	<1×10 <sup>1</sup>	Absent
PP 7	<1×10 <sup>1</sup>	<1×10 <sup>1</sup>	Absent
PP 8	<1×10 <sup>1</sup>	<1×10 <sup>1</sup>	Absent
PP 9	<1×10 <sup>1</sup>	<1×10 <sup>1</sup>	Absent
PP 10	<1×10 <sup>1</sup>	<1×10 <sup>1</sup>	Absent
PP 11	<1×10 <sup>1</sup>	<1×10 <sup>1</sup>	Absent
PP 12	1.6×10 <sup>2</sup>	<1×10 <sup>1</sup>	Absent
PP 13	<1×10 <sup>1</sup>	<1×10 <sup>1</sup>	Absent
PP 14	<1×10 <sup>1</sup>	<1×10 <sup>1</sup>	Absent
PP 15	<1×10 <sup>1</sup>	<1×10 <sup>1</sup>	Absent
PP 16	<1×10 <sup>1</sup>	<1×10 <sup>1</sup>	Absent
PP 17	<1×10 <sup>1</sup>	<1×10 <sup>1</sup>	Absent
PP 18	1.51×10 <sup>3</sup>	8.3×10 <sup>2</sup>	Absent
PP 19	8×10 <sup>1</sup>	<1×10 <sup>1</sup>	Absent
PP 20	<1×10 <sup>1</sup>	<1×10 <sup>1</sup>	Absent
PP 21	<1×10 <sup>1</sup>	<1×10 <sup>1</sup>	Absent
PP 22	3.2×10 <sup>2</sup>	<1×10 <sup>1</sup>	Absent
PP 23	<1×10 <sup>1</sup>	<1×10 <sup>1</sup>	Absent
PP 24	<1×10 <sup>1</sup>	<1×10 <sup>1</sup>	Absent
PP 25	<1×10 <sup>1</sup>	<1×10 <sup>1</sup>	Absent

Abbreviations: CFU: Colony-forming unit; PP: Pediatric product; TAMC: Total aerobic microbial count; TYMC: Total yeast and mold count.

**Table 4. TAMC and TYMC in cutaneous pediatric drug products**

No. of cutaneous PPs	TAMC (CFU per g or mL)	TYMC (CFU per g or mL)	Absence/presence of <i>Staphylococcus aureus</i> or <i>Pseudomonas aeruginosa</i> (per g or mL)
PP 1	<1×10 <sup>1</sup>	<1×10 <sup>1</sup>	Absent

Abbreviations: CFU: Colony-forming unit; PP: Pediatric product; TAMC: Total aerobic microbial count; TYMC: Total yeast and mold count.

satisfactory manufacturing hygiene and effectiveness of implemented quality control measures.

#### 4. Discussion

Regardless of dosage forms or route of administration, non-sterile pediatric drugs must adhere to the microbiological

purity standards established in the 2022 IP. PDPs can be broken down or rendered inactive by a variety of microbes, more specifically by the metabolites they produce.<sup>19</sup> Furthermore, because these medications are consumed by pediatric patients with immature immune systems, it is particularly important to ensure compliance with pharmacopeial requirements to prevent drug-related infections. Manufacturers of pediatric pharmaceuticals have recently improved the standard of non-sterile pediatric products to the point that they now report low levels of bioburden.<sup>20</sup>

However, in 2022, the World Health Organization (WHO) issued a global alert regarding four cough syrups that were suspected to be associated with the deaths of 66 children in The Gambia. It stated that the syrups were “possibly associated with major kidney damage as well as 66 deaths among children.” The medications were recognized by the WHO as Magrip N Cold syrup, Kofexmalin baby cough, Makoff baby cough syrup, and Promethazine oral solution. WHO issued a warning that using them could cause serious injury or even death, especially to children.<sup>21</sup>

This research aimed to investigate the presence of microbiological contaminants in non-sterile pediatric PPs available at local pharmacies in Ghaziabad, India. We assessed the microbiological quality of these pediatric drug products. The most widely utilized pediatric products include syrups, suspensions, emulsions, and solutions. Children, newborns, and infants respond to medications differently from adults. As children’s immune systems are underdeveloped, extra caution must be used when using pediatric medications to prevent potential infections. In this study, 25 commercially available pediatric syrups and one commercially available cream were examined, confirming the overall good microbiological quality. Of 26 PDPs tested, 23 complied with microbiological limit specifications set by both the IP and the EP and hence were found safe for use in the pediatric population. These 23 aqueous and cutaneous PDPs met the permissible limits for non-sterile preparations, with TAMC values of <1 × 10<sup>2</sup> CFU/mL and TYMC values of <1 × 10<sup>1</sup> CFU/mL.

Taking into account the findings of the microbiological evaluation shown in Tables 3 and 4, PP 18 demonstrated non-compliance, with a TAMC of 1.51×10<sup>3</sup> CFU/mL and a TYMC of 8.3 × 10<sup>2</sup> CFU/mL. In addition, PP 12 and PP 22 demonstrated non-compliance, with TAMC values of 1.6 × 10<sup>2</sup> and 3.2 × 10<sup>2</sup> CFU/mL, respectively. Thus, PP 12, PP 18, and PP 22 did not meet the acceptance criteria of the IP and EP, and their microbiological quality may have been compromised, rendering them unsafe for consumption by children, particularly those with compromised immune

systems. Suboptimal manufacturing practices, inadequate preservation, or improper handling during distribution and storage may be potential causes of this contamination. To prevent microbiological growth in diluted oral liquid drugs, strict hygiene practices are necessary throughout the production process.

This study highlights the importance of microbiological quality control in PDPs. The adoption of good preservative agents, rigorous quality control measures, and current GMP may account for the low level of microbial contamination in the analyzed samples of syrup and cream. The compliance rate of approximately 88% suggests that the Indian pharmaceutical industry, particularly in pediatric dosage forms, has made substantial progress in adopting rigorous quality control measures. These practices help maintain low microbial contamination, thereby protecting the health and safety of pediatric patients, who are particularly vulnerable. Consistently maintaining microbiological quality also reflects positively on the quality assurance systems and facilities of the pharmaceutical manufacturing units in the region.

Before being made available for consumption, non-sterile pharmaceutical preparations must pass testing for the presence of certain specified microorganisms (e.g., *E. coli*, *S. aureus*, and *P. aeruginosa*) in addition to bioburden tests, as recommended by the IP and EP. All the PDPs tested met the IP and EP standards and were confirmed to be devoid of specified microorganisms. This underscores the importance of adhering to strict quality assurance and current GMP in the production of such preparations.<sup>10,11</sup>

*E. coli*, which can cause serious illness in children, was found to be absent in aqueous PDPs, implying that the raw materials, manufacturing environment, and handling practices were in a sanitary state. Likewise, ensuring the absence of *P. aeruginosa*—an opportunistic microorganism that can be especially lethal in immunocompromised patients—in the cutaneous PDP indicates strong microbial control measures in these formulations. *S. aureus*, an organism associated with serious skin infections and commonly found in the nasal flora, was also not detected in the tested PDPs.<sup>15</sup>

The findings revealed that three PDPs (PP 12, PP 18, and PP 22) were contaminated, with microbial levels exceeding the acceptable limits. The possible sources of contamination include production equipments, water, or infected personnel. Detection of contamination in these three products indicates that although general industry practice is commendably high, there is still a need for ongoing surveillance, root-cause analysis, and corrective measures to address any remaining lapses. These findings also underscore the importance of microbiological

quality checks in finished formulations to ensure public health safety.

These results emphasize the microbial safety and regulatory compliance of the tested PDPs, which is particularly essential given the susceptibility of the pediatric population to microbial infections. This study highlights the need for proper utilization of preservatives, process validation, and robust environmental monitoring programs to limit microbial invasion during manufacture and storage. Microbiological monitoring at regular intervals throughout the entire product shelf life is still warranted to maintain this degree of safety.

## 5. Conclusion

The current investigation on the microbiological quality control of non-sterile PDPs demonstrates satisfactory microbiological safety of the products tested. The majority were in compliance with pharmacopeial requirements. However, three pediatric drug products exceeded the microbiological limits, thereby reflecting lapses in microbial quality control, particularly in terms of total viable counts. The failure of these three PDPs highlights the need for regular microbiological testing, staff training, environmental monitoring, and verification of cleaning and sanitization procedures. Therefore, to help preserve and improve the quality of PDPs in the Indian market, regulatory agencies should strengthen post-marketing surveillance and monitoring programs, enforce GMP, and implement more stringent marketing authorization procedures.

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## Conflict of interest

The authors declare they have no competing interests.

## Author contributions

*Conceptualization:* Anil Kumar Teotia, Prasad Thota, Vivekanandan Kalaiselvan

*Formal analysis:* Deeksha Verma, Prasad Thota

*Investigation:* Manoj Pandey

*Methodology:* Prasad Thota, Manoj Pandey

*Writing—original draft:* Deeksha Verma

*Writing—review & editing:* Deeksha Verma, Prasad Thota, Sanjay Mendiratta

**Ethics approval and consent to participate**

Not applicable.

**Consent for publication**

Not applicable.

**Availability of data**

Not applicable.

**References**

- Gholizadeh-Hashjin A, Lotfipour F, Hallaj-Nezhadi S. Quality control of non-sterile drug product according to United States' pharmacopeia instruction. *Iran J Med Microbiol.* 2019;13(5):321-345.  
doi: 10.30699/ijmm.13.5.321
- Poy MJC, Ramírez CC, Di Lauro SXG, *et al.* Microbiological quality of pediatric oral liquid formulations. *Farm Hosp.* 2016;40(5):427-435.  
doi: 10.7399/fh.2016.40.5.10541
- Olaitan MO, Muhammad B. Assessment of microbiological quality of syrup and water used in pharmaceutical industries in Kano State, Nigeria. *Ife J Sci.* 2018;20(1):119.  
doi: 10.4314/ijss.v20i1.12
- Khana M, Singh Y, Meenal Khana C, Teotia U. Effect of storage on microbial quality of non-sterile liquid dosage form. *J Pharmacog Phytochem.* 2018;7(2):479-481.
- Khanom S, Kanta Das K, Noor R, Banik S. *Microbiological Analysis of Liquid Oral Drugs Available In Bangladesh*; 2013. Available from: <https://www.researchgate.net/publication/256324356> [Last accessed on 2025 Aug 01].
- Murtaza G, Ahmed Khan M, Zeb-Un-Nisa M, Shafiq S. A review on the microbial contamination in the non-sterile pharmaceutical products. *Pharm Sci Technol.* 2021;5(2):68.  
doi: 10.11648/j.pst.20210502.17
- El-Houssieny RS, Aboulwafa MM, Elkhatib WF, Hassouna NAH. Recovery and detection of microbial contaminants in some non-sterile pharmaceutical products. *Arch Clin Microbiol.* 2013;4(6):1-14.  
doi: 10.3823/278
- Al-kaf AG, Alghalibi SM, Edrees WH. Microbial and physicochemical assays of paracetamol in different brands of analgesic syrups sold in Sana'a City-Yemen. *J Pharm Pharmacogn Res.* 2015;3(1):6-12.  
doi: 10.56499/jppres14.026\_3.1.6
- Thota P. "Prevalence of microbial contaminants in non-sterile pharmaceutical antacids." *Biomed J Sci Tech Res.* 2023;50(3):41695-41700.  
doi: 10.26717/bjstr.2023.50.007959
- Indian Pharmacopoeia Commission. *Microbial Contamination in Nonsterile Products.* 8<sup>th</sup> ed. Vol. 2.2.9. Uttar Pradesh: Indian Pharmacopoeia Commission; 2022. p. 40-52.
- Indian Pharmacopoeia Commission. *Microbiological Examination of Nonsterile Products: Microbial Enumeration Tests and Examination of Non-Sterile Products: Test for Specified Microorganisms.* 11<sup>th</sup> ed. Uttar Pradesh: Indian Pharmacopoeia Commission.
- Myemba DT, Bwire GM, Sangeda RZ. Microbiological quality of selected local and imported non-sterile pharmaceutical products in Dar es Salaam, Tanzania. *Infect Drug Resist.* 2022;15:2021-2034.  
doi: 10.2147/IDR.S355331
- Taysir Alsaleem A, Faihan Obaid AH, Olayan Alribi Alruwaili R, *et al.* Investigation of the Microbial Contamination of Pharmaceutical Products. *Lett High Energy Phys.* 2023;23(4):421-436.
- Conway J, Bero L, Ondari C, Wasan KM. Review of the quality of pediatric medications in developing countries. *J Pharm Sci.* 2013;102(5):1419-1433.  
doi: 10.1002/jps.23474
- Sudeshika SHT, Panagoda GJ, Tennakoon IUK. Microbiological quality of paediatric oral liquid drug formulations during consumption. *Int J Sci Res Publ.* 2014;4(9):2.
- Opoku S, Nyanor I. Qualitative and quantitative microbiological studies of paediatric artemether-lumefantrine dry powders and paracetamol syrups obtained from selected drug stores in Accra, Ghana. *J Trop Med.* 2019;2019:7062016.  
doi: 10.1155/2019/7062016
- Buhlmann X. *Method for Microbiological Testing of Nonsterile Pharmaceuticals.* Vol. 16. 1968. Available from: <https://journals.asm.org/journal/am> [Last accessed on 2025 Aug 01].
- McKinnon BT, Avis KE. IRIMER membrane filtration of pharmaceutical solutions. *Am J Hosp Pharm.* 1993; 50:1921-1936.  
doi: 10.1093/ajhp/50.9.1921
- Ratajczak M, Kubicka MM, Kamińska D, Sawicka P, Długaszewska J. Microbiological quality of non-sterile pharmaceutical products. *Saudi Pharm J.* 2015;23(3):303-307.  
doi: 10.1016/j.jsps.2014.11.015
- Gamal M, Sangar B. *Microbial Evaluation of Some Non-Sterile Pharmaceutical Preparations Commonly Used at Al-Khoms Market, Libya.* Vo. 8. 2019. Available from: <https://www.com/internationalscholarsjournals.org> [Last accessed on 2025 Aug 01].
- WHO. *WHO Alert Over India-Made Cough Syrups after Deaths in The Gambia.* United States: BBC.