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Microbiological Analysis of Pharmaceutical Non Injectable Drugs Produced in Dhaka, Bangladesh

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Abstract

Pharmaceutical drugs are applied and consumed by the patients with weak immune system and for this reason these products must be of good quality and within the required microbiological limit. Present study attempted to determine the microbiological quality of pharmaceutical non injectable oral and topical drugs as well as their antibacterial activity. A total of sixty samples were studied from different categories of medicine including syrup, tablet & capsule and ointments. Microbiological analysis was done after serial dilution. Antibacterial activity of the samples was also determined by Kirby-Bauer method. The total viable bacterial count of 9 syrups, 7 tablet & capsules and 13 ointments samples exceeded the microbial limit <102cfu/ml or cfu/gm recommended by USP (United States Pharmacopeia) and BP (British Pharmacopeia). Regarding to the presence of specific bacteria, about six, six and three samples from syrup, tablet & capsule and ointment samples were of good quality respectively out of twenty samples each. Some drug prevailed good activity towards few bacteria and no activity at all to some others. As the drugs possess antibacterial activity, the contaminants might represent some other species of the same genera of bacteria having some mechanisms to prohibit such activities towards them. More than 50% of the drugs contain higher bacterial and fungal load rendering the quality at risk and not recommended to use by the patients to whom these products will impart most harm as these patients are already immune compromised.

Keywords: Pharmaceutical Drugs; Syrup; Ointments; Tablets; Contamination; Antibacterial Activity

Abbreviations: FDA: Food and Drug Administration; GMP: Good Manufacturing Practice; USP: United States Pharmacopeia; BP: British Pharmacopeia; NA: Nutrient Agar; TVC: Total Viable Count; USP: United States Pharmacopeia.

Introduction

To obtain the quality products in a pharmaceutical company, it is necessary to control all stages of drug production, which covers all matters influencing the quality of a product, including raw materials, the manufacturing process and the evaluation of finished product [1]. Primarily, the microbial quality of pharmaceutical products depends on the quality of raw materials, production process, production environment, hygiene of the personnel involved in manufacture and the storage conditions. Some other factors for contamination include faulty manufacturing and packaging process [2,3]. The presence of pathogenic microorganisms and the presence of relatively high number non-pathogenic microorganisms are objectionable in pharmaceutical products [4]. Among many types of pharmaceutical products, syrups are non- sterile liquid dosage which contain active medicaments and constitute the most convenient dosage for all ages but mostly prepared for oral administration in children since tablets and capsules cannot be easily or conveniently administered to them [5,6].

The United States Food and Drug Administration (FDA) require that drug product be tested for its purity, identity, strength, quality and stability before it can be released for use. Hence pharmaceutical validation and process control are important [7]. In non-sterile pharmaceutical preparations, the incidence of microbes is influenced by the nature of ingredients (raw materials), the quality of the vehicle, and the care and attitude of personnel involved in their handling including tablets oral dosage forms are not required to be sterile, but certain quality control measures are essential to keep the microbial content of these preparations safe and acceptable [8]. The extent of microbial contamination in tablets is usually influenced by the microbiological quality of the starting raw materials, packaging materials, personnel that come in contact with the product during the manufacturing process and the production environment as well as equipment. Failure to observe Good Manufacturing Practice (GMP) at any stage of production may consequently affect the microbiological quality of the product. Contaminants entrapped into the product via the above mentioned routes may not survive for a long period of time due to the lethal effect exerted by the various methods used in tablet production [9,10]. Basically, medicines get spoiled by initial or early pioneer invaders of biodegrading microorganisms, which prepare the way for later invaders, by degrading complex nutrients, altering the surrounding pH and making more moisture available [11,12]. Though pharmaceutical industries are growing fast in Bangladesh, the quality of drugs is being compromised due to unlicensed industries and competitive marketing [13]. So it is necessary to check microbiological quality of pharmaceutical products to assure consumer safety.

Therefore, microbiological assessment of the product and the knowledge of pathogen-specific antibiotic resistance are important. Similar studies were done for different pharmaceutical products in Bangladesh where on an average 50% products exceeded the microbial limit by USP (United States Pharmacopeia) and BP (British Pharmacopeia) with complete absence of *Salmonella spp*. [14,15]. But in current context we studied with a large sample volume to check if the condition has improved or not. Current study was attempted to understand the current scenario of non-injectable pharmaceutical products like syrup, tablet & capsule and ointments along with antibacterial activity against some common microorganisms.

Materials and Methods

Sample Collection and Preparation

Seventy samples (Syrup-20, Tablet & Capsule-20, Ointment-20) were collected from different types of medicinal stores. All samples were tested to assess the bacterial and fungal load as well as to detect the presence of specific pathogenic bacteria and actinomycetes, using the standard microbiological and biochemical methods [16-20].

Dilution of Sample

For homogenized sample, serial dilution of all the pharmaceutical samples was done individually. 10 fold serial dilutions were then prepared by transferring one ml of the original well homogenized sample to a tube containing 9 ml of sterile normal saline and so forth until 10^{-5} dilution was obtained. Each test tube was labeled with the type of sample and number of the dilution.

Enumeration of Total Viable Bacterial and Fungal Count

An aliquot of 0.1 ml of each suspension from the dilution 10^{-2} was spread onto nutrient agar (NA) plate and Sabouraud dextrose agar (SDA) plate for enumerating total viable count (TVC) and total fungal load respectively [21-26]. The plates were incubated at 37˚C for 24 hours (NA plates) and at 25˚C for 48 to 72 hours (SDA plates).

Enumeration of Specific Pathogens

From the dilution of 10^{-2} of each sample, 0.1 ml of suspension was spread onto MacConkey agar, mannitol salt agar (MSA), cetrimide agar, and SS agar media for the enumeration of *Escherichia coli*, *Klebsiella* spp., *Staphylococcus* spp., *Pseudomonas* spp., *Salmonella* spp. and *Shigella* spp. consecutively. All the plates were incubated at 37oC for 24 hours. Presence of *E. coli* was further confirmed by the appearance of bluish-black colonies with green metallic sheen on the eosine-methylene blue (EMB) agar [24]. Confirmative biochemical tests were carried out for the final identification of the isolates [16,20,24].

Determination of Antimicrobial Activity of the Samples

The antibacterial activity of the samples was performed following the agar well diffusion method [27,28]. The suspension of the samples was used directly on the Mueller-Hinton agar media. At first, the pathogenic bacterial suspensions with 0.5 McFarland turbidity (*Pseudomonas* spp, *Vibrio* spp, *Salmonella* spp, *Klebsiella* spp, *Staphylococcus aureus*, *Proteus* spp., *Enterobacter* spp., *Acinetobacter* spp.) were inoculated over the Mueller-Hinton agar media separately using cotton swab and 100 µl of the suspension of drug samples were introduced into the wells made in the agar plates using sterile cork borer with a positive control

(antibiotic disc) and a negative control (normal saline). Presence of clear zone around the wells filled with the sample solution indicated the antibacterial activity of tested samples.

Results

Much heterotrophic bacterial growth was observed within the pharmaceutical products in the current study. For syrup samples as well as tablet and capsule samples, the total bacterial count ranged from 1.0×10^2 cfu/unit to 9.2×10^4 cfu/unit (Tables 1 & 2). Ointment samples showed growth of total aerobic bacteria with lowest count in sample 18 of about 1.8×10^2 cfu/gm to 8.9×10^4 cfu/gm (Table 3) in sample 6 and 14 respectively. Raw materials also harbored aerobic bacteria ranging from 2.4×10^2 cfu/gm in milk of magnesia to 2.7×10^4cfu/gm in magnesium chloride (Table 4). *Escherichia coli* was absent in all of the 70 samples. Most prevalent contaminants found in all of the products include *Staphylococcus aureus* (highest count in tablet & capsules), *Pseudomonas spp*. (highest count in syrup samples as well as tablet & capsule samples) and *Klebsiella* spp. (highest in sample 4 of tablet and capsule). Raw materials tested in this study were free from *Salmonella* spp. but some of the finished products like syrup, tablet & capsule, ointments were found to be contaminated with *Salmonella* spp. Syrup samples 12 and 20 were free from specific organisms even though they contain higher total bacterial count. Total 6 samples out of 20 (1, 5, 9, 14, 15, 18) were found to be in approvable range for consumer safety compared to other samples. Sample no 6, 7, 8, 9, 10 and 18 of tablet & capsule were under the recommended microbial limit [16,29]. Only 3 ointment samples were of good quality here (Tables 5 & 6).

Sample	TVB (cfu/g)	Total fungal count	*E. coli* (cfu/ml)	*Klebsiella spp. (cfu/ml)*	*Salmonella* spp. (cfu/ ml)	*Pseudomonasspp. (cfu/ ml)*	*Staphylococcusspp. (cfu/ ml)*
1. Magmil	3.5×10^2	2.5×10^1	-	-	-	2.0×10^2	5.3×10^2
2. Benmet	5.5×10^2	4.6×10^1	-	2.0×10^3	-	2.0×10^2	5.5×10^2
3. Suzel	2.0×10^2	-	-	3.3×10^3	-	-	3.0×10^2
4. Megalax	1.0×10^3	-	-	-	-	-	2.0×10^2
5. Gavisol	1.8×10^2	-	-	8.0×10^2	-	-	1.8×10^2
6. Nactar	1.6×10^2	3.3×10^1	-	1.0×10^2	-	1.1×10^3	3.0×10^2
7. Cremag	2.7×10^3	-	-	1.1×10^2	-	1.8×10^2	3.6×10^2
8. Laxefin	1.3×10^3	2.1×10^1	-	3.0×10^2	1.3×10^3	1.2×10^4	-
9. Flustar	1.8×10^2	-	-	6.6×10^2	-	1.0×10^2	-
10. Cosy	2.2×10^4	-	-	2.0×10^2	-	3.2×10^4	-
11. Nitaxide	1.0×10^2	-	-	2.7×10^2	-	1.3×10^3	-
12. Anthel	9.2×10^4	-	-	-	-	-	-
13. Zesup	2.5×10^2	1.3×10^1	-	-	-	-	1.0×10^3
14. Visocid	1.2×10^2	6.0×10^1	-	-	1.3×10^3	-	1.8×10^2
15. Orsal	6.8×10^2	5.2×10^1	-	-	-	-	1.6×10^2
16. Bercef	2.7×10^3	4.2×10^1	-	1.7×10^2	-	2.7×10^3	2.7×10^3
17. Macorax	1.3×10^3	-	-	7.0×10^3	-	1.3×10^3	1.3×10^3
18. Magfin	1.8×10^2	-	-	1.8×10^2	-	-	1.8×10^2
19. Ceflon	2.2×10^4	1.1×10^1	-	1.6×10^2	-	-	2.2×10^4
20. Tuspel	2.7×10^3	1.1×10^1	-	-	-	-	-

*TVB= Total Viable Bacteria

Table1: Prevalence of Pathogenic Microorganisms in Syrup.

Sample	TVB (cfu/g)	Total fungal count	*E. coli* (cfu/g)	*Klebsiella* spp. (cfu/g)	*Pseudomonas* spp. (cfu/g)	*Staphylococcus* spp. (cfu/g)
1. Metfo	2.2×10^4	2.1×10^1	-	3.3×10^3	-	4.1×10^3
2. Tramic	1.0×10^2	-	-	5.8×10^2	3.9×10^3	1.3×10^3
3. Imet	9.2×10^4	-	-	2.7×10^3	6.8×10^2	6.8×10^2
4. Aduvit	9.2×10^4	-	-	9.7×10^4	-	2.7×10^3
5. Poidone	6.1×10^2	-	-	-	2.7×10^4	6.7×10^4
6. Gaston	4.3×10^2	3.3×10^1	-	-	1.3×10^3	-
7. Comet	-	4.2×10^1	-	-	-	-
8. Cal D	-	2.1×10^1	-	-	-	-
9. Rabprazo	-	2.2×10^1	-	-	-	-
10. 1- VITA	-	-	-	-	-	-
11. AC PR	1.2×10^2	-	-	-	-	2.7×10^3
12. Arilol	6.8×10^2	-	-	3.3×10^3	-	6.7×10^4
13. Baclof	3.2×10^2	1.3×10^1	-	-	1.3×10^3	8.9×10^4
14. Caltrol	1.2×10^2	6.0×10^1	-	2.7×10^3	6.8×10^2	3.6×10^4
15. Amdova	6.8×10^2	5.2×10^1	-	6.7×10^4	2.7×10^3	2.1×10^2
16. Diatrol	2.7×10^3	-	-		6.7×10^4	3.7×10^2
17. Lipigent	1.3×10^3	-	-		-	-
18. Olmesan	1.8×10^2	-	-		-	-
19. Atova	2.9×10^4	1.1×10^1	-	-	-	-
20. Lisinopril	3.1×10^3	1.1×10^1	-	-	-	-

*TVB= Total Viable Bacteria

Table 2: Prevalence of Pathogenic Microorganisms in Tablet & Capsule.

Sample	TVB cfu/g)	Total fungal count	*E. coli* (cfu/g)	*Klebsiella* spp. (cfu/g)	*Pseudomonas* spp. (cfu/g)	*Staphylococcus* spp.(cfu/g)
1. E-Burn	8.7×10^3	-	-	-	-	-
2. Xzema	1.3×10^3	-	-	-	-	-
3. Cosmotrin	6.8×10^2	-	-	-	-	4.0×10^2
4. Avison	2.7×10^3	-	-	-	2.7×10^4	2.8×10^2
5. Neostan	6.7×10^4	1.6×10^1	-	-	1.3×10^3	3.0×10^2
6. Xencort	8.9×10^4	-	-	8.9×10^2	3.8×10^2	-
7. Cetaphil	3.6×10^4	-	-	5.5×10^2	5.7×10^4	4.7×10^2
8. Exovate	2.1×10^2	-	-	3.0×10^2	1.3×10^3	-
9. Gentosep	3.7×10^2	2.2×10^1	-	2.4×10^2	-	
10. Nebanol	-	1.1×10^1	-	1.2×10^3	-	2.0×10^2
11. Miki-H	-	-	-	3.0×10^2	-	4.7×10^2
12. Remus	-	-	-	-	-	1.2×10^2

13. Usidin	2.5×10^4	1.3×10^1	-	-	-	5.3×10^2
14. Lomexin	8.9×10^4	6.0×10^1	-	-	-	-
15. Amela	3.6×10^4	5.2×10^1	-	5.6×10^2	-	-
16. Emulsifying ointment	6.7×10^4	4.2×10^1	-	4.7×10^2	-	-
17. Pevison	1.3×10^3	2.1×10^1	-	-	-	-
18. Pevaryl	1.8×10^2	-	-	-	-	-
19. Clopirox	3.1×10^4	-	-	-	-	-
20. Turboclav	7.2×10^3	-	-	-	-	-

*TVB= Total Viable Bacteria.

Table 3: Prevalence of Pathogenic Microorganisms in Ointments.

Sample	*Vibrio* spp	*Salmonella* spp	*Pseudomonas* spp	*S. aureus*	*Proteus* spp.	*Klebsiella* spp	*Enterobacter* spp	*Acinetobacter* spp
1. Magmil	13 mm	0 mm	13 mm	0 mm	0 mm	0 mm	11 mm	11 mm
2. Benmet	12 mm	16 mm	12 mm	0 mm	19 mm	0 mm	12 mm	13 mm
3. Suzel	0 mm	0 mm	0 mm	23 mm	13 mm	0 mm	0 mm	0mm
4. Megalax	10 mm	10 mm	10 mm	17 mm	0 mm	12 mm	0 mm	13 mm
5. Gavisol	12 mm	0 mm	12 mm	0 mm	0 mm	14 mm	12 mm	15 mm
6. Nactar	15 mm	0 mm	15 mm	0 mm	15 mm	15 mm	0 mm	0 mm
7. Cremag	12 mm	23 mm	12 mm	0 mm	16 mm	0 mm	0 mm	9 mm
8. Laxefin	21 mm	17 mm	8 mm	0 mm	12 mm	0 mm	12 mm	7 mm
9. Flustar	20 mm	0 mm	0 mm	14 mm	0 mm	12 mm	14 mm	9 mm
10. Cosy	10 mm	0 mm	15 mm	13 mm	0 mm	15 mm	14 mm	12 mm
11. Nitaxide	25 mm	0 mm	0 mm	18 mm	0 mm	16 mm	12 mm	8 mm
12. Anthel	9 mm	0 mm	0 mm	9 mm	13 mm	0 mm	13 mm	12 mm
13. Zesup	17 mm	14 mm	15 mm	0 mm	17 mm	12 mm	15 mm	14 mm
14. Visocid	16 mm	13 mm	16 mm	12 mm	0 mm	17 mm	16 mm	0 mm
15. Orsal	19 mm	18 mm	12 mm	11 mm	0 mm	0 mm	0 mm	8 mm
16. Bercef	17 mm	20 mm	13 mm	13 mm	12 mm	0mm	0 mm	14 mm
17. Macorax	0 mm	17 mm	16 mm	0 mm	14 mm	0 mm	0 mm	0 mm
18. Magfin	16 mm	0 mm	17 mm	10 mm	0 mm	0 mm	0 mm	0 mm
19. Ceflon	14 mm	16 mm	0 mm	18 mm	17 mm	0mm	0 mm	12 mm
20. Tuspel	19 mm	12 mm	0 mm	13 mm	13 mm	0 mm	0 mm	0 mm

Table 4: Antimicrobial Activity of Syrup Sample.

All of the twenty syrup samples showed some degree of antimicrobial properties against several bacterial isolates. The average zone of inhibition was 15 mm. highest activity was showed against *Vibrio* spp. (Sample 8-21 mm, sample 9-20 mm, sample 11-25 mm) and *Salmonella* spp. (sample 7-23 mm, sample 16-20 mm). Antibacterial activity against other isolates showed similar results with syrup samples.

Sample	*Vibrio* spp	*Salmonella* spp	*Pseudomonas* spp	*S. aureus*	*Proteus* spp.	*Klebsiella* spp	*Enterobacter* spp	*Acinetobacter* spp
1. Metfo	0 mm	0 mm	0 mm	0 mm	9 mm	13 mm	0 mm	13 mm
2. Tramic	15 mm	0 mm	0 mm	0 mm	23 mm	13 mm	0 mm	0 mm
3. Imet	0 mm	0 mm	10 mm	10 mm	17 mm	0 mm	12 mm	0 mm
4. Aduvit	10 mm	15 mm	0 mm	12 mm	0 mm	0 mm	14 mm	12 mm
5. Poidone	0 mm	16 mm	0 mm	15 mm	0 mm	15 mm	15 mm	0 mm
6. Gaston	15 mm	12 mm	23 mm	12 mm	0 mm	16 mm	0 mm	0 mm
7. Comet	11 mm	0 mm	17 mm	8 mm	0 mm	12 mm	0 mm	12 mm
8. Cal D	13 mm	0 mm	0 mm	0 mm	14 mm	0 mm	12 mm	14 mm
9. Rabprazo	14 mm	0 mm	0 mm	15 mm	13 mm	0 mm	15 mm	14 mm
10. 1- VITA	14 mm	13 mm	0 mm	0 mm	18 mm	0 mm	16 mm	12 mm
11. AC PR	15 mm	0 mm	0 mm	0 mm	9 mm	13 mm	0 mm	13 mm
12. Arilol	9 mm	12 mm	14 mm	15 mm	0 mm	17 mm	12 mm	15 mm
13. Baclof	17 mm	0 mm	13 mm	16 mm	12 mm	0 mm	17 mm	16 mm
14. Caltrol	0 mm	12 mm	18 mm	12 mm	11 mm	0 mm	0 mm	0 mm
15. Amdova	0 mm	10 mm	20 mm	13 mm	13 mm	12 mm	0mm	0 mm
16. Diatrol	0 mm	24 mm	0 mm	0 mm	0 mm	0 mm	15 mm	11 mm
17. Lipigent	0 mm	0 mm	0 mm	15 mm	12 mm	0 mm	14 mm	0 mm
18. Olmesan	16 mm	9 mm	0 mm	16 mm	12 mm	0 mm	0 mm	12 mm
19. Atova	14 mm	12 mm	12 mm	12 mm	0 mm	0 mm	0 mm	11 mm
20. Lisinopril	19 mm	11 mm	12 mm	0 mm	0 mm	0 mm	0mm	0 mm

Table 5: Antimicrobial Activity of Tablet & Capsule Sample.

With tablet and capsule sample, lowest number of samples had antimicrobial activities against *Klebisella* spp. just as like the syrup samples did. Highest effectivity was found with sample 2 for Proteus spp. (23 mm). Such high activity was also found for sample 6 and 15 against *Pseudomonas* spp. (23 mm and 20 mm respectively), sample 16 against *Salmonella* spp. (24 mm), and sample 20 against *Vibrio* spp. (19 mm).

Sample	*Vibrio* spp	*Salmonella* spp	*Pseudomonas* spp	*S. aureus*	*Proteus* spp.	*Klebsiella* spp	*Enterobacter* spp	*Acinetobacter* spp
1. E-Burn	0 mm	0 mm	0 mm	13 mm	16 mm	0 mm	12 mm	0 mm
2. Xzema	0 mm	12 mm	0 mm	0mm	0 mm	24 mm	0 mm	12 mm
3. Cosmotrin	0 mm	15 mm	0 mm	13 mm	0 mm	13 mm	0 mm	0 mm
4. Avison	10 mm	10 mm	0 mm	12 mm	16 mm	12 mm	0 mm	19 mm
5. Neostan	12 mm	12 mm	16 mm	0 mm	0 mm	0 mm	23 mm	13 mm
6. Xencort	0 mm	0 mm	12 mm	10 mm	10 mm	10 mm	17 mm	0 mm
7. Cetaphil	0 mm	12 mm	0 mm	12 mm	0 mm	0 mm	0 mm	0 mm
8. Exovate	9 mm	8 mm	0 mm	15 mm	0 mm	15 mm	0 mm	15 mm
9. Gentosep	20 mm	0 mm	0 mm	12 mm	23 mm	0 mm	0 mm	0 mm
10. Nebanol	10 mm	15 mm	13 mm	21 mm	17 mm	8 mm	0 mm	30 mm
11. Miki-H	14 mm	0 mm	17 mm	20 mm	0 mm	0 mm	14 mm	0 mm

12. Remus	9 mm	0 mm	0 mm	10 mm	0 mm	15 mm	13 mm	0 mm
13. Usidin	15 mm	15 mm	0 mm	25 mm	0 mm	0 mm	18 mm	0 mm
14. Lomexin	0 mm	16 mm	12 mm	9 mm	0 mm	0 mm	9 mm	13 mm
15. Amela	0 mm	12 mm	0 mm	17 mm	14 mm	15 mm	0 mm	17 mm
16. Emulsifying ointment	17 mm	13 mm	0 mm	16 mm	13 mm	16 mm	12 mm	0 mm
17. Pevison	0 mm	0 mm	0 mm	19 mm	18 mm	12 mm	11 mm	0 mm
18. Pevaryl	16 mm	0 mm	0 mm	17 mm	20 mm	13 mm	13 mm	12 mm
19. Clopirox	14 mm	15 mm	0 mm	0 mm	17 mm	16 mm	0 mm	14 mm
20. Turboclav	19 mm	0 mm	12 mm	16 mm	0 mm	17 mm	10 mm	0 mm

Table 6: Antimicrobial Activity of Ointment Sample.

Lowest antimicrobial activity was seen against *Salmonella* spp. and *Pseudomonas* spp. On an average better antibacterial activity was showed against *Staphylococcus aureus*, *Proteus* spp. and *Klebsiella* spp.

Discussion

The purpose of this experiment was to determine the presence of microorganisms in finished pharmaceuticals products such as syrup, tablet & capsule, ointment, raw materials etc. It is quite disappointing that all the products were contaminated with several kinds of bacteria and fungi as well. Total aerobic bacterial load was within 10^4 cfu/gm or cfu/ml and total fungal count did not exceed 10^1 cfu/gm or cfu/ml. Other than these, *Klebsiella* spp., *Pseudomonas* spp., *Staphylococcus aureus* and even *Salmonella* spp. were present abundantly which were not supposed to be present to some samples like ointments. Nine syrup samples crossed the USP (United States Pharmacopeia) limit of total aerobic bacterial count of $<10^2$ cfu/ml making these products unsatisfactory to be used by patients. Topical ointments and aqueous preparations for oral use (syrups) must not contain *Pseudomonas* spp. and *Staphylococcus aureus* according to USP. The load of *Klebsiella* spp. must be not more than 10^2 cfu/gm which already exceeded in several samples (3 syrup samples, 6 tablet & capsule samples). The non-aqueous oral drugs (tablet & capsule) which were contaminated with *Klebsiella* spp., the load for all of these samples were more than the acceptable limit. The quality of the products is really at a stake to be used by the patients. As the pharmaceutical products under this study were not sterile products, they can have some bacteria but within a particular range of course. In addition to that there will be no pathogenic specific bacterial count which were already found to be present in the test samples [16,29]. As medicines are provided to the patients who are already diseased and in a immune suppressive condition due to the disease, administration of such contaminated drugs may cause a serious damage in them compared to healthy individuals. Samples can be contaminated in different ways in industrial sectors such as during handling of raw materials, water, processing of products, unclean machineries, contaminated packaging materials, storage condition of the packaging and raw materials etc. To ensure the safety of people it is necessary to identify the source of contamination related to such drugs. In industrial sectors, workers hygiene who directly works in mixing and production area is one of the most important factors to control.

Besides microbiological analysis, syrup, tablet and capsule as well as ointments samples were subjected for antimicrobial activity testing against some laboratory freeze dried pathogenic bacterial isolates. Some samples showed no activity at all and some showed good antibacterial activity up to 24 mm. *Vibrio* spp. and *Salmonella* spp. showed best results with the drugs and *Enterobacter* spp. showed the least results. As *Vibrio* spp. and *Salmonella* spp. both have some pathogenic species, they showed good results by showing larger zone of inhibition. Antibacterial activity against other bacteria was also found out to be average activity of around 15 mm. As all of the oral drugs (syrup, tablet and capsule) possess some antibacterial activity, the products themselves are contaminated with some bacteria which fall under the same genera of classification but the species might be different so that the presence of bacteria and the inhibiting bacteria might be affected differently by these drugs. Same scenario is applicable for ointments as well. There is less risk with contamination as these products are not administered orally and the route of entry of all the bacteria might not be skin. But while applying the ointments in broken skin with exposed blood, the bacteria might get disseminated within the body with blood circulation.

Conclusion

Present study revealed a huge amount of heterotrophic microbes as well as some specific bacteria which are

beyond the accepted limit according to USP (United States Pharmacopeia) and BP (British Pharmacopeia). However, stringent regulatory actions on the microbiological quality control along with the personal hygienic improvement during formulation, handling, and storage of products would be effective for the better management of overall public health situation. Besides strict regulation and law enforcement must be applied by the government to control such production of bad quality pharmaceutical products.

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