



## Research Article

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## Determination of Microfungal Contamination in Some Used Oral Liquid Pharmaceuticals

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Received: 31 January 2017

Revised: 01 March 2017

Accepted: 08 March 2017

### ABSTRACT

In this study, it was aimed to determine of Microfungal contamination in some used oral liquid pharmaceuticals. 25 different oral liquid pharmaceuticals were used. 1ml of liquid pharmaceutical from each was taken to inoculate with Rosebengal Chloramphenicol Agar and Sabouraud Dextrose Agar medium. Inoculated petri dishes were incubated for two weeks at 27°C. As a result of incubation, a colony of *Alternaria alternata* was isolated from only number 8 sample and Rosebengal Chloramphenicol Agar medium. Microfungal growth was not observed in other samples and on Sabouraud Dextrose Agar medium. Oral liquid pharmaceuticals have been found to be highly clean regarding Microfungal contamination. This demonstrates that good manufacturing practices are followed, that certain substances contained in liquid pharmaceuticals do not allow fungal growth, and that liquid pharmaceuticals are well maintained during use.

**Keyword:** Microfungi; microfungal contamination; oral liquid pharmaceuticals; public health

### INTRODUCTION

Oral liquid pharmaceuticals are one of the commonly used drug forms in the treatment of various diseases and disorders. It is especially preferred in children, who have difficulty in swallowing, and cannot use solid forms of medicine. Syrups are liquid pharmaceuticals containing high concentrations of sugar. Polyols such as glycerin and sorbitol are added to improve flavour, prevent crystallisation and change the solubility. Preservatives such as nipa esters, sodium benzoate and sorbic acid are also added to protect against fermentation and mould [1-3].

Microbial contamination in oral liquid pharmaceuticals arises when hygiene rules are not fully complied during production, storage and use. Oral pharmaceuticals can contain a

small number of microorganisms. However, if they contain pathogenic microorganisms, they can cause infections and various health problems. Also, toxic metabolites and cell fractions of microorganisms can produce different clinical patterns [4-13].

Oral liquid pharmaceuticals lose their sterility when they are opened for use and become suitable for contamination. The hygienic nature of the environment (e.g., home, office, hospital) increases the risk of microbial contamination. As a result, different health problems can be encountered while healing is expected. Therefore, this issue has a great importance for individual and community health. This research aims to determine Microfungal contamination in

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some oral liquid pharmaceuticals that have been used but not yet expired.

## MATERIALS AND METHODS

### Sampling and inoculation

In this study, 25 different oral liquid pharmaceutical products were used whose the expiry dates have not been over. Commercial names, active ingredients and the using area of the pharmaceutical products are set out in Table 1. Inoculation was made to each of the pharmaceutical products by using surface spreading technique [3,4,12] into the Rosebengal Chloramphenicol Agar (RbCA) and Sabouraud Dextrose Agar (SDA) media by using 1 ml of sterile pipettes for each sample separately.

### Incubation and identification

Inoculated petri dishes were incubated for two weeks at 27°C. The developing microfungus colony was transferred to a petri dish containing Malt Extract Agar (MEA) and incubated at 27°C for two weeks. After incubation, macroscopic and microscopic examinations were performed and diagnosed according to the relevant references [14-17].

## RESULTS AND DISCUSSION

Nearly all oral liquid pharmaceuticals used in our research were found to be clean regarding microfungus contamination. In the medium containing RbCA, only 1 colony was isolated from number 8 sample and was identified as *Alternaria alternata* (Fr.) Keissler. Microfungus

growth was not observed in other samples and SDA medium (Table 1).

We believe that the preservatives and high sugar levels in the liquid pharmaceuticals prevent microfungus growth. We can also say that good manufacturing practices are complied with during the production phase and are well maintained during use. We believe that the isolated *A. alternata* is infected because of the human body or during the use of the pharmaceutical product. Similar comments have been made in related references [1-4].

*Alternaria* species are mostly planted parasites, and the most common species is *A. alternata*. It is a common dematiaceous fungus that is frequently isolated from indoor air, food, soil and plants [14-18]. In humans, *A. alternata* infections occur as opportunistic pathogens in immunocompromised individuals. *Alternaria* species can lead to different diseases such as allergies, skin infections, soft tissue infections, brain abscesses and respiratory infections [17-18].

The presence of fungi in oral liquid pharmaceuticals, which can produce such different clinical tabulations in humans, has a great importance regarding individual and community health. There is always a risk of microbial contamination, especially during use, even if preservatives are used in liquid pharmaceutical products. This means that the individual and environmental hygiene rules must be strictly followed and kept in proper condition until the date of last consumption.

**Table 1: The features of liquid pharmaceuticals and distributions of microfungi**

Sample No.	Commercial Name	Effective Agent	Using Area	Microfungal distribution	
				RbCA*	SDA*
1	A-ferin Plus	Parasetamol, Chlorfeniramin maleate, Pseudoefedrin HCl	Upper respiratory tract infections	-	-
2	Andorex	Benzidamine hydrochloride, Klorheksidin glukonat	Oral antiseptic, Upper respiratory tract infections	-	-
3	Assist	Acetylcysteine	Upper respiratory tract infections, Lower respiratory tract infections	-	-
4	Atarax	Hydroxyzine hydrochloride	Antihistaminic	-	-
5	Bricanyl	Terbutaline sulphate, Guaifenesin	Upper respiratory tract infections, Lower respiratory tract infections	-	-
6	Calpol	Paracetamol	Analgesic, Antipyretic	-	-
7	Chinko	Chinkosulfate heptahydrate	Zinc deficiency, Immune support	-	-
8	Gaviscon	Alginic acid, Aluminum hydroxide, Sodium bicarbonate	Reflux, ulcer, gastritis	<i>Alternari alternata</i> 1 colony	-
9	Hitrizin	Cetirizine hydrochloride	Antihistaminic	-	-
10	Iburamin	Ibuprofen, Pseudoephedrine, Chlorpheniramine maleate	Upper respiratory tract infections, Lower respiratory tract infections	-	-
11	Kloroben	Benzidamine hydrochloride, Chlorhexidine gluconate	Oral antiseptic, Upper respiratory tract infections	-	-
12	Kreval	Butamyrat citrate	Upper respiratory tract infections, Lower respiratory tract infections	-	-
13	Metpamid	Methoclopyramide HCl	Nausea, Vomiting, Reflux, Ulcer	-	-
14	Mucolytic Pediatric Syrup	Carbocysteine	Lower respiratory tract infections	-	-
15	Notuss Fort	Butamyrat citrate	Upper respiratory tract infections, Lower respiratory tract infections	-	-
16	Osmolak	Lactulose	Constipation, Laxative	-	-
17	Pedifen	Ibuprofen	Analgesic, Antipyretic, Anti-inflammatory	-	-
18	Perebron	Oxolamine phosphate	Upper respiratory tract infections, Lower respiratory tract infections	-	-
19	Pulmorest	Levodropropizin	Upper respiratory tract infections, Lower respiratory tract infections	-	-

20	Sekrol	Ambroxole hydrochloride	Upper respiratory tract infections, Lower respiratory tract infections	-	-
21	Sinecod	Butamirate citrate	Upper respiratory tract infections, Lower respiratory tract infections	-	-
22	Sudafed	Pseudoephedrine hydrochloride, Guaifenesin	Upper respiratory tract infections, Lower respiratory tract infections	-	-
23	Tanflex	Benzidamine hydrochloride	Upper respiratory tract infections	-	-
24	Tylo Cold	Paracetamol, Chlorpheniramine maleate, Dextromethorphan, Pseudoephedrine HCl	Upper respiratory tract infections, Lower respiratory tract infections	-	-
25	Ventolin	Salbutamol sulphate	Lower respiratory tract infections	-	-

**RbCA:** Rosebengal Chloramphenicol Agar

**SDA:** Sabouraud Dextrose Agar

## CONCLUSION

According to our results, oral liquid pharmaceuticals used in the research were found to be very clean regarding Microfungal contamination. *A. alternata* as a colony was isolated from only one sample. This suggests that oral liquid pharmaceuticals comply with the Good Manufacturing Practices (GMP) guidelines during the manufacturing phase and are properly maintained during use. Considering that even a single pathogenic microorganism can cause infection, it must be kept in good condition during use, and personal and environmental hygiene should be emphasised. Such studies should be done more and help to protect the health of the community.

## CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing interests.

## REFERENCES

1. Acartürk F, Ağabeyoğlu İ, Çelebi N, Değim T, Değim Z, Doğanay T, Takka S, Tırnaksız F. Modern Farmasötik Teknoloji. Ankara: Türk Eczacılar Birliği Eczacılık Akademisi Yayınları; 2. Baskı; 2009.
2. Ogbulie JN, Ibe IJ, Nguma CC. The microbial associates of unexpired and expired paediatric syrups. Nigerian J Microbiol 2009; 23(1): 1817-1822.
3. Abu Taha AS, Al-Shahed QN, Sweileh WM, Sawalha AF, Al-Naser AZ, Abu Zanat AO. The vulnerability of cough syrups marketed in Palestine to microbial challenge test. J Chem Pharm Res 2010; 2(5): 115-121.
4. Yıldırım S, Yel M. Farmasötik şurupların aerop bakteri sayısı, *Salmonella sp.* ve *Escherichia coli* yönünden araştırılması. Türk Hij Den Biyol Derg 2000; 57(2): 95-98.
5. Nwachukwu E, Olugbue V. Microbiological evaluation of ten commercial cough syrups during storage. Int J Biomed Pharm Sci 2009; 3(1): 69-73.
6. Gad GFM, Aly RAI, Ashour MSE. Microbial evaluation of some non-sterile pharmaceutical preparations commonly used in the Egyptian market. Trop J Pharm Res 2011; 10(4): 437-445.
7. Kamil OH, Lupuliasa D. Modern aspects regarding the microbial spoilage of pharmaceutical products. Farmacia 2011; 59(2): 133-146.
8. Emejuru MC, Ojiegbe GC, Azı S, Nwosu N.B.: the Microbiological load of selected oral liquid pharmaceuticals. Int J Comm Res 2013; 2(3): 39-45.
9. Khanom S, Das KK, Banik S, Noor R. Microbiological analysis of liquid oral drugs available in Bangladesh. Int Pharm Pharm Sci 2013; 5(4): 479-482.

10. 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 Pharmacog Res* 2015; 3(1): 6-12.
11. Fatema K, Chakraborty SR, Sultana T, Rahman M, Kamali NM, Das KK, Noor R. Assessment of microbiological quality of the paediatric oral liquid drugs. *J Pharmacog Phytochem* 2014; 3(1): 165-171.
12. Razvi N, Awan R, Naqvi BS, Anjum F, Hussain Z, Farooqi S. Estimation of microbial contamination in various active pharmaceutical ingredients and excipients. *World J Pharm Pharmaceut Sci* 2014; 3(6): 1771-1777.
13. Osungunna MO, Mba M, Adebajo O. Evaluation of microbial quality of selected blister-packed paracetamol tablets and paracetamol syrups marketed in Nigeria. *Afr J Clin Exper Microbiol* 2016; 17(2): 151-158.
14. Domsch KH, Gams W, Anderson TH. *Compendium of soil fungi*. London: Academic Press; 1980.
15. Hasenekoğlu İ. *Toprak mikrofungusları*. Cilt 1-7. Erzurum: Atatürk Üniversitesi Yayınları; 1991.
16. Ellis D, Davis S, Alexiou H, Handke R, Bartley R. *Descriptions of medical fungi*. 2<sup>nd</sup> ed. Adelaide: Nexus Print Solutions; 2007.
17. Refai M, El-Yazid HA. *Monograph on dematiaceous fungi*. Cairo: Cairo University; 2014.
18. Gürcan Ş, Pişkin S, Kılıç H, Temelli BA, Yalçın Ö. İmmün sistemi sağlam bir konakta *Alternaria alternata* ile oluşan deri enfeksiyonu. *Mikrobiyol Bul* 2009; 43: 163-167.

**Cite this article as:**

Vedat Kadir Özkan, Mustafa Tamer UZUN. Determination of Microfungal Contamination in Some Used Oral Liquid Pharmaceuticals. *J Pharm Chem Biol Sci* 2017; 5(1): 05-09