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Short communication

Disinfectant treatment in the production of cephalosporin oral pharmaceutical dosage forms

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Introduction

Cephalosporins are one of the most clinically significant classes of β-lactam antibiotics, in oral dosage forms — tablets, capsules, dry powder suspensions, and effervescent granules — constituting a substantial share of global antibiotic consumption. The manufacturing process introduces a unique set of microbial contamination and cross-contamination challenges that demand rigorous disinfection and decontamination protocols.

Regulatory agencies require that manufacturers of non-penicillin beta-lactam drugs, such as cephalosporins, to employ control strategies to prevent cross-contamination, thereby reducing the potential for life-threatening allergic reactions in patients. This mandate is codified under the Federal Food, Drug, and Cosmetic Act and enforced through Current Good Manufacturing Practice (cGMP) guidelines (FDA, 2013).

An analysis of regulatory agencies including EMA, FDA, Health Canada, ANVISA, CDSCO, PIC/S, and WHO reveals that the majority require beta-lactams (classified as sensitizing materials) to be produced in dedicated and segregated facilities. This segregation imperative makes disinfectant treatment a critical operational pillar in cephalosporin manufacturing.

Materials and methods

The performance of treatment with disinfectants on isolates, from the microbiological environmental monitoring of the area in the Production of cephalosporins, includes standard personal protective equipment and standard laboratory equipment: laminar flow cabinet class II, incubator at 30-35°C, Bunsen burner, Vortex mixer, pH meter, identification apparatus, automatic pipets, sterile Petri dishes, stainless steel coupons (5 cm x 5 cm), plain sterile swabs with plastic applicator Rayon tipped, laboratory accessories. Nutrient media used in the process: Casein soya bean digest agar, buffered sodium chloride-peptone solution, buffered sodium chloride-peptone solution with neutralizers, all in compliance with the current European Pharmacopoeia (Sandle, 2016).

The efficiency of these disinfectants in different concentration levels were examined: Solution 1 (5g Benzalkonium Chloride /100 ml) in concentration: 0,4% ; Solution 2 (10 g Benzalkonium Chloride /100 ml) in concentration: 1% ; Solution 3 (inorganic chlorine compound, Sodium Hypochlorite - NaClO) in concentrations: 2,0% and 4,0% ; Solution 4 (ready to use sporicidal disinfectant solution, containing 6% hydrogen peroxide). Solution 5, Denaturated Ethanol 70% *v/v* (ready to use).

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This paper analyzes the effectiveness of disinfectants on the following isolates from the monitoring of the cephalosporin production area: *Rothia kristinae, Micrococcus lylae and Bacillus simplex.*

Rothia kristinae – Gram-positive microorganism. The cells are coccoid which tend to group together as tetrads. It is slightly facultatively anaerobic. *Rothia kristinae* is a common human skin and oral microorganism but can cause opportunistic infections in humans.

Micrococcus lylae – Gram-positive, strictly aerobic microorganism. The normal habitat of it is skin, dust and water. It grows in tetrads, irregular clusters and cubical packets of eight and colonies are often brightly pigmented.

Bacillus simplex – an environmental microorganism found mainly in soil. Cells are Gram-variable rods, 0.7–0.9 μm in diameter, and motile. Endospores are ellipsoidal (occasionally spherical), positioned centrally. Colonies are cream, glossy, 3–6 mm in diameter after 2 days, with irregular margins and a slightly raised, umbonate appearance.

Method

On a sterile stainless steel "coupon" 5cm x 5cm, placed in a sterile Petri dish, 50 μL of test suspension of microorganism is applied (with a micropipette), on which the effectiveness of the disinfectant is tested (United States Pharmacopeial Convention, 2008). 50 μL of the examined disinfectant prepared "ex tempore" is applied over the test suspension of microorganism. The action of the disinfectants is examined in previously determined contact time intervals: 15 seconds, 30 seconds, 1 minute and 3 minutes contact time with the suspension of the microorganism and the disinfectant. After the specified time interval, the liquid from the stainless steel "coupon" is collected with a sterile swab, with several rotational movements until dry traces appear on the stainless steel "coupon". The Casein soya bean digest agars are incubated at a temperature of 30-35˚ C, 3-5 days. The results are quantified using the plate–count method. The growth is counted every 24 hours, and the results are obtained after 5 days of incubation.

Results and discussion

The results are presented as a percentage reduction of the colony- units of all tested in- house microorganisms determined for every concentration. The Efficiency of the disinfectant Solution 1 resulted in 100.00% reduction in all tested time intervals for all microorganisms. The Efficiency of the disinfectant Solution 2 resulted in 100.00% reduction in all tested time intervals for all microorganisms. The Efficiency of the disinfectant Solution 3 resulted in 100.00% reduction in all tested time intervals for all microorganisms. The Efficiency of the disinfectant Solution 4 resulted in 100.00% reduction in all tested time intervals for all microorganisms. The Efficiency of the disinfectant Solution 5 resulted in 100.00% reduction in all tested time intervals for *Micrococcus lylae* and *Rothia kristinae* and 98% reduction for *Bacillus simplex* at 15 seconds and 100% reduction at 30 seconds, 1 and 3 minutes.

Conclusion

By confirming the efficacy of the tested disinfectants against the selected microorganisms, it is concluded that disinfectant Solutions 1, 2, 3, and 4 ensured complete effectiveness, achieving 100.00% reduction across all tested time intervals for all microorganisms, thus demonstrating consistent and reliable antimicrobial activity.Disinfectant Solution 5 also exhibited high efficacy, achieving 100.00% reduction for *Micrococcus lylae* and *Rothia kristinae* across all tested time intervals, and 98% reduction for *Bacillus simplex* at 15 seconds, reaching 100.00% reduction at 30 seconds, 1 minute, and 3 minutes.

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