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Original Article

Enhanced antibacterial activity of Ciprofloxacin ocular inserts against *S. aureus* and *P. Aeruginosa*

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ABSTRACT

Background: Ciprofloxacin hydrochloride is a common antibiotic used for treating bacterial infections, and enhancing its antibacterial activity is considered a crucial concern of scientific researchers. **Objectives:** The objective of this work aim to show the enhancement of the antibacterial activity of ciprofloxacin ocular inserts against *P. aeruginosa and S. aureus.* **Method:** The enhancement of antibacterial activity of ciprofloxacin ocular inserts against *P. aeruginosa* and *S. aureus* was evaluated using microbiological susceptibility tests. The inserts composed of two types of spray-dried matrices, SD_1 and SD_2. **Results:** Promising results were obtained and the two formulae were found to be effective against *S. aureus* and *P. aeruginosa*, also the results indicated clear zones of inhibition every day up to seven days. **Conclusion:** It was concluded that ciprofloxacin hydrochloride is a good antibacterial agent.

Keywords: Ciprofloxacin HCl, Ocular Inserts, Antibacterial Activity, Microbiological Susceptibility Test.

Introduction

Ciprofloxacin hydrochloride (CFX-HCl) as a commercially available antibiotic is used for treating bacterial infections in various parts of the body [1, 2]. It does not work only for viral infections, but it has imperative applications in treating various ocular illnesses, such as corneal ulcers and bacterial conjunctivitis, although the regimen is tedious [3]. It can treat chronic bacterial prostatitis, urinary tract infections, acute uncomplicated cystitis, and acute sinusitis [4, 5]. This antibiotic is the prototype member of the fluoroquinolones antibiotics. It has both Gram-negative and -positive activities, which start by interference with replication and transcription of DNA via the inhibition of bacterial DNA gyrase/topoisomerase II and DNA topoisomerase IV, thus, prevention unwinding and duplication of bacterial DNA [6].

Access this article online	
Website: www.japer.in	**E-ISSN:** 2249-3379

How to cite this article: Samar Z. Alshawwa. Enhanced Antibacterial Activity of Ciprofloxacin Ocular Inserts against *S. aureus* and *P. Aeruginosa*. J Adv Pharm Educ Res. 2020;10(4):132-4. Source of Support: Nil, Conflict of Interest: Declared.

Pseudomonas aeruginosa is an opportunistic organism, which is prevalent in water, it is a classic opportunistic pathogen as it initiates resistance to many disinfectants and antibiotics, besides its armory of putative virulence factors plasmid acquired resistance [7]. It is the most common gram-negative organism that is found in nosocomial infections leading to various infections, especially in immunecompromised, neutropenic, burns/tissue injury and cystic fibrosis patients all over the world [8]. Since the majority of *P. aeruginosa* strains are resistant to most of the antibacterial agents, they are considered as one of the major problems in many hospitals because of its high rates for developing resistance against most of the antimicrobial agents [9]. Ciprofloxacin was particularly effective against the Enterobacteriaceae [10]. It was previously reported by Chalkley and Koornhof that ciprofloxacin is effective against *E. coli* and *P. aeruginosa*. The bactericidal effect was achieved immediately after the addition of 0.5 µg/ml of ciprofloxacin, culture viability was reduced from 5×10^5 to about 5×10^3 CFU/ml within 15 min, and at a concentration of 0.1 µg/ml, a larger than a 10-folds reduction in viability resulted during the first hour after exposure [11].

Enhancing the antibacterial effect of ciprofloxacin against *P. aeruginosa* was recently considered one of the major concerns of scientific researchers. The effect of combining Nimesulide with

ciprofloxacin on the enhancement of its antibacterial activity was studied by Abiramietal in 2015 and promising results were obtained [12]. On the other hand, Masadeh et al in 2016 reported that pretreating the bacterial cells with vorinostate could enlarge the inhibition zones and minimizes the minimum inhibitory concentration [13]. Also pretreating the bacterial cells with agents having antioxidant properties such as tempol, melatonin, and pentoxifylline enhances the antibacterial activity of ciprofloxacin as reported by Masadeh et al in 2016 [14]. Another group of researchers reported that ciprofloxacin-loaded Lipid-Core nanocapsules (LNC) with a mean size of 180 nm showed similar minimum inhibitory concentrations as the free drug in *P. aeruginosa* and *S. aureus* The treatment of *S. aureus* with free ciprofloxacin leads to the formation of biofilm-like aggregates that can be avoided by exposure to LNC. Ciprofloxacin-loaded LNC with combined advantages compared to the non-encapsulated drug represents a promising drug delivery system with the prospect of improving antibiotic therapy in patients with cystic fibrosis [15].

The aim of this work was to show the enhancement of the antibacterial activity of ciprofloxacin ocular inserts against *S. aureus* and *P. aeruginosa*.

Materials and Methods

The antimicrobial activity of CFX-HCl (Biocon, India) ocular inserts was studied by carrying out microbiological susceptibility tests. The release of CFX-HCl from the inserts was investigated bacteriologically in agar plates seeded with *P. aeruginosa* 27853 and *S. aureus* 25925. Two spray-dried matrices SD_1 and SD_2 were studied.

The suspension for spray drying was prepared by gradual addition of carbopol (C-934) (Shanghai, China) suspension into xanthan gum (Shanghai, China) suspension and efficient stirring to prevent lump formation. As a second step both propylene glycol (PG) (Shanghai, China) and CFX-HCl were added to the suspension, and finally deionized water was added to continue the volume to the required. The prepared suspension was spray-dried with (BUCH I 190) spray dryer to give the matrices SD_1 and SD_2 having the compositions shown in (Table 1).

Table 1: Composition of the spray-dried matrices.

Formula	XG	C-934	CFX-HCl	PG
SD1	0.5%	0.5%	0.5%	0%
SD2	0.5%	0.5%	0.5%	0.5%

Results and Discussion

The results in (Table 2) and (Table 3) show that all formulae were found to be effective against *P. aeruginosa* and *S. aureus*. Where the inhibition zones diameters produced in the spray-dried matrices SD_1, SD_2, and CFX-HCl standard both in the powder or solution forms were all similar or comparable to each other indicating that CFX-HCl in all formulae is available for ocular absorption. Results also showed that the excipients in the formulae did not produce inhibition zones so they were biologically inactive, interaction zones are produced mainly by the powder form where the drug is considered highly concentrated.

The inhibition zone diameter produced by the powder was up to 7 days. The results in (Table 2) indicated clear zones of inhibition every day up to 7 days, meaning that CFX-HCl exhibited a constant controlled release from the ocular inserts. It is obviously observed that the inhibition zones produced by SD_2 were of greater diameter than SD_1, which could be due to a diffusion effect because of the presence of PG in the formula.

Table 2: Inhibition zones diameter produced by suspension (mm).

Formula	P. aeruginosa		S. aureus	
	Test	Reference	Test	Reference
SD_2	35.3±0.6	35.3±0.6	28.3±0.6	27.7±0.6
SD_1	33.3±1.2	33.0±1.0	29.2±0.8	29.7±1.2
Free drug- SD_2	0.0±0.0		0.0±0.0	
Free drug- SD_1	0.0±0.0		0.0±0.0	
Inhibition zones diameter produced by powder forms (mm)				
SD_2	42.0±0.0	47.0±0.0	36.0±0.0	39.3±0.6
SD_1	40.8±0.8	49.0±0.0	34.5±0.5	41.0±0.0

Table 3: Inhibition zones diameter produced by powder forms (mm) for 7 days.

Inhibition zones diameter produced by powder forms (mm)					
Hours	Formula	P. aeruginosa		S. aureus	
		Test	Reference	Test	Reference
24	SD_2	43.0	47.0	35.5	38.5
	SD_1	43.0	50.0	35.0	39.0
48	SD_2	42.0	48.0	35.0	38.5
	SD_1	43.0	49.0	36.0	40.0
72	SD_2	42.0	48.0	36.0	38.0
	SD_1	43.0	48.0	36.0	39.0
96	SD_2	43.0	49.0	35.5	39.0
	SD_1	43.0	49.0	36.0	39.0
7^{th} day	SD_2	43.0	49.0	35.0	39.0
	SD_1	43.0	50.0	37.0	40.0

Conclusions

Formulae SD_1 and SD_2 were found to be effective against *P. aeruginosa* and *S. aureus*. It could be concluded that CFX-HCl is a potent antibacterial agent, and it could be successfully administered through controlled release of ocular inserts for the treatment of bacterial keratitis and conjunctivitis.

List of abbreviations:

Symbol	Abbreviation
C-934	Carbopol
CFX-HCl	Ciprofloxacin Hydrochloride
PG	Propylene Glycol
SD	Spray Dried
XG	Xanthan Gum

Conflict of interest:

The author confirms that the content of this article has no conflict of interest

Acknowledgements:

This research was funded by the Deanship of Scientific Research at Princess Nourah bint Abdulrahman University through the Fast-track Research Funding Program. Special thanks to the team of doctors Aiman Obaidat, Alsayed Sallam, and Mutaz Sheikh Salem for their valuable support.

Patient consent

Declared none.

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