

EVALUATION OF THE PHARMACEUTICAL CHARACTERISTICS OF ARTIFICIAL TEARS

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Abstract

The eye is an essential organ, very sensitive and delicate. The diseases that can reach the eye are numerous, among them being with a quite high frequency a condition called dry eye syndrome or dry keratoconjunctivitis.

The objective of the study is to optimize an artificial tear formula and pharmaceutical characterization to be well tolerated when applied on the conjunctiva.

The use of artificial tears has a certain limitation, because human tears have a complex behavior, whereas artificial tears cannot completely replace them.

Special attention is paid to the preparation of ophthalmic preparations for obtaining drugs with good tolerability in the eye area. Tolerability is dependent on therapeutic efficacy, determining optimal bioavailability.

We obtained 6 formulas of artificial tears based on 940 carbomer neutralized with NaOH 10% and triethanolamine respectively.

After preparation, the pH, the refractive index, the density and the viscosity were determined for the artificial tears.

The formula containing 0.3% carbomer 940 shows the physical characteristics specific to the ophthalmic preparations specified in the compendial prevision.

Key words: ophthalmic preparations, artificial tears, carbomer 940

INTRODUCTION

One of the characteristics of the eyeball is the surface covered by the tear fluid, which the eyelids continuously display, preventing the drying of the exposed part of the air and facilitating the closing of the eyelids.

Dry eye syndrome is a disease of which a large part of the population suffers, its prevalence is between 5 - 35%, depending on the age group: 5.7% in women under 50; 9.8% women over 75; and 3.9% in men 50-54 years old; 7.6% in men over 80 years.(Cerenea P., 2002)

Thus, the quality of the vision and the daily activities are affected, being difficult to diagnose because there is no correlation between symptoms and signs; there are no standardized tests and well-defined

criteria for diagnosis.(Nilforoushan M.R et al., 2005)

Artificial tears were created to meet this irritant syndrome, which through their highly effective properties have given good results. (Calvaosantos G.et al., 2011; McCann L.C et al. 2012) It is the most effective method in the treatment of dry eye.

The ocular mucosa has a special sensitivity that is accentuated during the treatment period, the ocular lesions have a strictly local specificity.(Hayati F et al.,2018)

These ocular pharmaceutical forms, must be formulated in such a way as to mimic natural tears, as far as their components and action are concerned.(Moshirfar M. et al., 2014)

MATERIAL AND METHOD

Materials: The components used are of adequate purity, attested by analysis bulletins issued by the manufacturer: Carbomer 940 (Elton Corporation SA Romania), triethanolamine (Merck KgaA, Germany, lot K49471379), sodium hydroxide (CHEM 118109252, Nordic Chemicals SRL, Romania), ethyl alcohol (Coman Product Romaina, lot 27649). The water was purified by distillation to be of physico-chemical and sterile purity. (FR X, 2018; PhEur 9th, 2017)

Preparation of artificial tear formulas:

To achieve the proposed objective, respectively of obtaining an artificial tears formula, we developed and evaluated six formulas based on Carbomer 940, dispersed in hydro-alcoholic mixtures and neutralized with triethanolamine, respectively NaOH (Tabel 1).

Tabel 1.

Components	Artificial tears formulas					
	T ₁	T ₂	T ₃	N ₁	N ₂	N ₃
Carbomer 940	0,1 g	0,2g	0,3 g	0,1 g	0,2 g	0,3 g
Ethyl alcohol	2,00 g	2,00 g	2,00 g	2,00 g	2,00 g	2,00 g
NaOH 10%	-	-	-	1,00 g	2,00 g	3,00 g
Triethanolamine	0,1 g	0,2 g	0,3 g	-	-	-
Propyl p-hydroxy benzoate	0,01 g	0,01 g	0,01 g	0,01 g	0,01 g	0,01 g
Distilled water	100,00 g	100,00 g	100,00 g	100,00 g	100,00 g	100,00 g

Three solutions of different concentrations of triethanolamine were prepared (formula T1 concentration 0.1%, formula T2 concentration 0.2%, formula T3 concentration 0.3%) and three solutions with NaOH 10% (formula N 1 concentration 0.1%, formula N 2 concentration 0.2%, formula N3 concentration 0.3%).

After preparation, the artificial tears were conditioned in containers corresponding to the physical state (Lupuliasa D. et al., 2019; Popovici I. et al., 2011).

Characterization of the artificial tear formulation:

In the evaluation of artificial tears I appreciated physicochemical properties.

Measurements were performed at 33°C, which corresponds to the temperature of the ocular surface. (Acara D. et al, 2018)

The pH of the formulas was determined at room temperature with a pH-meter calibrated (model Inolab 7310 with electrode SenTix 81 Plus). The refractive index and density were measured with an Optika Abbe 2 WA Refractometer, respectively a calibrated ISOLAB picnometer, at 22°C.

To determine the rheological properties of the six tear formulas we used the Visco Ball viscometer, with a drop ball for transparent Newtonian liquids. All measurements were performed in triplicate.

RESULTS AND DISCUSSION

The formulations in which the neutralization with NaOH 10% was performed are presented as clear liquids, with a low viscosity (formulas N1, N2), and the formula N3 has a higher viscosity.

In the case of formulas neutralized with Triethanolamine (formulas T1, T2, T3) they are homogeneous, and the viscosity increases in increasing order of the concentration of triethanolamine.

In formula T1 we observe a slightly viscous liquid form, in formula T2 we notice an increase in viscosity, and in formula T3 we obtained a homogeneous and transparent hydrogel.

The refractive index determined with respect to the environment (air), is expressed as the ratio of the speed of light in the environment and the speed of light absorbed by the preparation.

The refractive index values of artificial tear formulas are presented in table 2.

Tabel 2

Characteristics of artificial tears

Formulas artificial tears	Refraction index	pH	Density (g/cm ³)
T ₁	1,3345	8,0	0,984
T ₂	1,3349	8,0	0,969
T ₃	1,3350	7,5	1,128
N ₁	1,3349	8,5	0,986
N ₂	1,3350	8,5	0,994
N ₃	1,3351	8,5	0,996

Density determinations were used to assess the viscosity of artificial tear formulas.

The pH value of the tear fluid is 7.4 (7.35 - 7.95); however, the pH values tolerated by ocivariate were experimentally determined to be between 7.5 and 9.5; slightly alkaline solutions being better tolerated by the eye than acidic ones.

The pH values of the artificial tears we obtain are included within these limits.

In assessing the viscosity of artificial tears, the dynamics of rotation and falling of the ball through the cylindrical tube were taken into account, slightly inclined and filled with the sample to be analyzed during the fall. [24]

The balls are borosilicate glass, Ni-Fe alloy, stainless steel with diameter and density specified in the technical data sheet of the viscometer. The viscosity values are included in the table 3.

Tabel 3

The rheological characteristics of artificial tears

Formulas artificial tears	Constance of the bile mPa.s. cm³/g.s	Fall time t(s)	Result
N₁	0,007	30,58	0,259
N₂	0,007	81	0,683
N₃	0,09	460	49,845
T₁	0,09	227	145,379
T₂	4,5	330	9995,53
T₃	4,5	335	9998,21

We mention that in the literature the tears have a viscosity that should not exceed the limit of 40-50mPa·s [2, 3], so the only artificial tear formula that meets this requirement is N3 having a viscosity of 49,845 mPa·s.

CONCLUSIONS

Artificial tears are used in irritant eye and dry eye syndromes, conditions in which the amount of water in the tear fluid decreases.

The results obtained in this study have shown that the formulation of artificial tears in situ based on carbomer 940 has properties suitable for ophthalmic topical administration.

Formula N3 due to the physical and rheological characteristics (viscosity of 49,845 mPa·s) has a better tear film recovery potential being better tolerated.

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