



ULBS

Universitatea "Lucian Blaga" din Sibiu



Interdisciplinary PhD School

PhD Domain: **Medicine**

ABSTRACT OF PhD THESIS

**A NEW THERAPEUTICAL
APPROACH IN DRY EYE DISEASE**

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ABSTRACT

Dry eye disease (DED) represents one of the most widely spread pathologies of the ocular surface. Dry eye is defined as a “multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles”. The main symptoms of dry eye mentioned are: soreness, burning, grittiness, watery eyes and visual disturbing that can affect one or both eyes.

The objectives of the treatment for DED are the ones related to increasing the patients' quality of life. This aspect can be accomplished by reducing the symptoms, correcting the Meibomian gland dysfunctions, restoring the tear film both quantitatively and qualitatively, and restoring the tear film homeostasis.

The presented thesis consists of a general part “*The current state of knowledge*”, in which general elements regarding the tear film's structure, DED definition, classification, diagnostic methods and treatment are presented. General aspects of pharmaceutical development and Quality by design, a modern concept used in pharmaceutical industry in order to develop a good product, are presented in the last chapter of the general part. This concept was successfully applied in the second chapter of the special part.

The experimental work of the thesis, “*Personal contribution*”, comprises the synthesis of the PhD research. The first step was to analyze the management of DED in the pharmacies from Sibiu County. The second study concerns the formulation and evaluation of the characteristics of a dietary supplement used by patients with dry eye disease, applying the Quality by Design concept. The last study had as a main objective the formulation and stability evaluation of a serum with hyaluronic acid, with topical application, in the periorbital zone.

For a better systematization of the presented information, the thesis includes a number of 28 figures and 18 tables. The last chapter presents the original elements and the innovations which are brought by this thesis.

The results obtained during the doctoral research were published in three articles and were presented by taking part at national conferences and congresses.

The innovation elements of this thesis are presented in chapters 6 and 7, which present the pharmaceutical development of new products, with a new composition which has not been described before in the literature. The main objective of this work was to assist the patients with DED.

The orodispersible tablets obtained through direct compression have many advantages in the pharmaceutical industry, being easy to obtain, well tolerated by patients with swallowing difficulties. The quality profile of the developed product is certified by the results of the mechanical properties of the analyzed tablets. All the five formulations had good results for the disintegration time, and according to the European Pharmacopeia 9.0 – “*orodispersible tablets should disintegrate in less than 3 minutes*”, the best results were recorded for the “B” formula which contains only sodium carboxymethylcellulose as a disintegrating agent.

In this paper a dietary supplement with natural ingredients was formulated for the first time, conditioned as orodispersible tablets, a new pharmaceutical dosage form which comes with multiple advantages for the needs of patients, being easy to administer.

The risk assessment analysis for developing this new product represents an element of novelty by applying solid pharmaceutical technology principles, establishing the quality profile of the desired product first, and then studying the influence of formulation factors, which can affect the quality of the developed product.

Another element of novelty is represented by the serum developed in chapter 7, which is one with a unique composition. The molecules of hyaluronic acid and bilberry liquid extract used as active ingredients bring direct benefits to the patients with DED.

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ABBREVIATION LIST

DED – dry eye disease

TFOS –Tear Film and Ocular Surface Society

DEWS –International Dry Eye Workshop

AR – retinoic acid

OTC – over the counter medicines

FDA – Food and Drug Administration

OSDI – Ocular Surface Disease Index

DEQ5 – Dry Eye Questionnaire 5

CMC - carboxymethyl cellulose

HPMC – hydroxypropylmethyl cellulose

HA – hyaluronic acid

FI – internal phase

QbD – Quality by Design

EMA – European Medicines Agency

QTPP – quality target profile

CQAs – critical quality attributes

CCS – sodium croscarmellose

CRP – crospovidone

PP – polypropylene

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