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Benevolent Approach of *In Vitro* And *Ex Vivo* Study in Ayurvedic Ocular Therapeutics

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Abstract

Animal Experimentation like in vitro and in vivo study plays an important role in research and understanding the ocular delivery system. Any new drug development is carried out on cell culture. Tissue engineering has developed biologically equivalent replacements which are used for research. Topical therapies in the form of kriyakalpa are widely used in netra roga chikitsa. There are multiple studies available regarding the results of kriyakalpa. It is need of hour to prove its mode of action, ocular drug delivery, safety, efficacy and toxicity of ayurvedic ocular medicines on modern parameters. If proven; ayurvedic ocular therapeutics will be globally accepted. Many ocular therapeutics give temporary symptomatic relief, in such conditions alternative ayurvedic treatment modality can be developed using cell culture study. In vitro and ex vivo models of the conjunctiva, cornea, vitreous, retina, etc can play an important role in research and development of ayurvedic ophthalmic drug. This review summarizes various available cell models, their uses and limitations. This can be helpful for further research in ayurvedic ocular drug delivery system.

Keywords: *Experimental Study (In Vitro And In Vivo), Kriyakalpa, Ocular Toxicity, Ocular Drug Delivery.*

1. Introduction

Research and development of ophthalmic drugs and ocular delivery systems both heavily rely on animal testing. [1] in the anterior and posterior segments of the eye, ocular barriers play an important part in controlling and regulating the inward and outward transport of solutes, fluids, and also administered drugs. Upon topical administration to the anterior part of the eye, drug molecules are prevented from reaching their ocular site of action as a result of anterior static barriers (i.e., tight junctions of corneal epithelium [CE] and blood–aqueous barriers) and also anterior dynamic barriers (i.e., lacrimal drainage and tear fluid barrier, conjunctival blood and lymphatic clearance). In addition, posterior ocular tissue hinders drug permeation due to expression of efflux pumps on the cell membrane and also by the presence of static and dynamic barriers. [2] Research-use replacements that are biologically equivalent have been created through tissue engineering. In netra roga chikitsa, topical treatments in the form of kriyakalpas are frequently employed. Regarding the outcomes of kriyakalpa, there are numerous studies available. It is urgent to demonstrate the ayurvedic eye medications' mode of action, method of drug delivery, safety, effectiveness, and toxicity using contemporary standards. Ayurvedic ocular therapeutics will be widely accepted if they are proven. Numerous ocular therapeutics only provide momentary symptom relief; in these cases, an alternative ayurvedic treatment method can be developed using cell culture research. Conjunctiva, cornea, vitreous, retina, and other in vitro and ex vivo models of these tissues can be useful in the development of ayurvedic ophthalmic drugs.

Recently constructed ocular models of conjunctiva, cornea, vitreous, retina and ex vivo models with their advantages, limitations are the key aspects of our study.

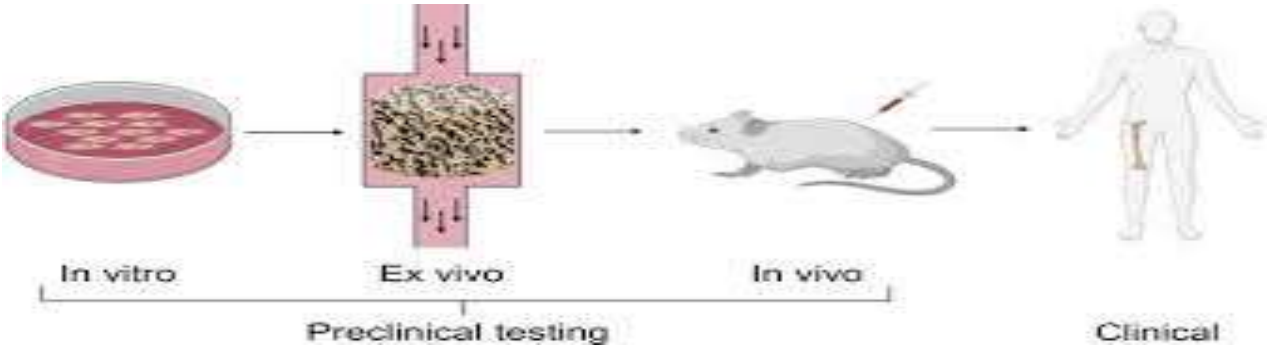


Figure-1

Table 1 [3] In Vitro Conjunctival Models Derived from Primary Cells

Species.	**TEER (Ω cm2).**	**Application(s)**
	Primary	
Rabbit~	1900	Active transport studies and permeability
Rabbit~	1100	Transport studies and metabolism
Cow~	5600	Toxicity studies
	Immortalized	
Conjunctival (HCjE) cell line		Ocular surface defence mechanism

Table 2 [4]Summary of the Corneal Epithelial Models

Species.	**Application(s)**
Primary.	Active transport studies and permeability
Rabbit.	Permeability studies
Rabbit.	Ocular irritation, toxicity, and drug absorption
Human Immortalized SIRC.	Corneal drug metabolism and transport
Epiocular.	Ocular sensitivity and corrosion
SkinEthic.	Ocular sensitivity and corrosion
Clonetics.	Ocular irritation and transepithelial permeability studies

Table- 3 [5] Vitreous Experimental Substitutes

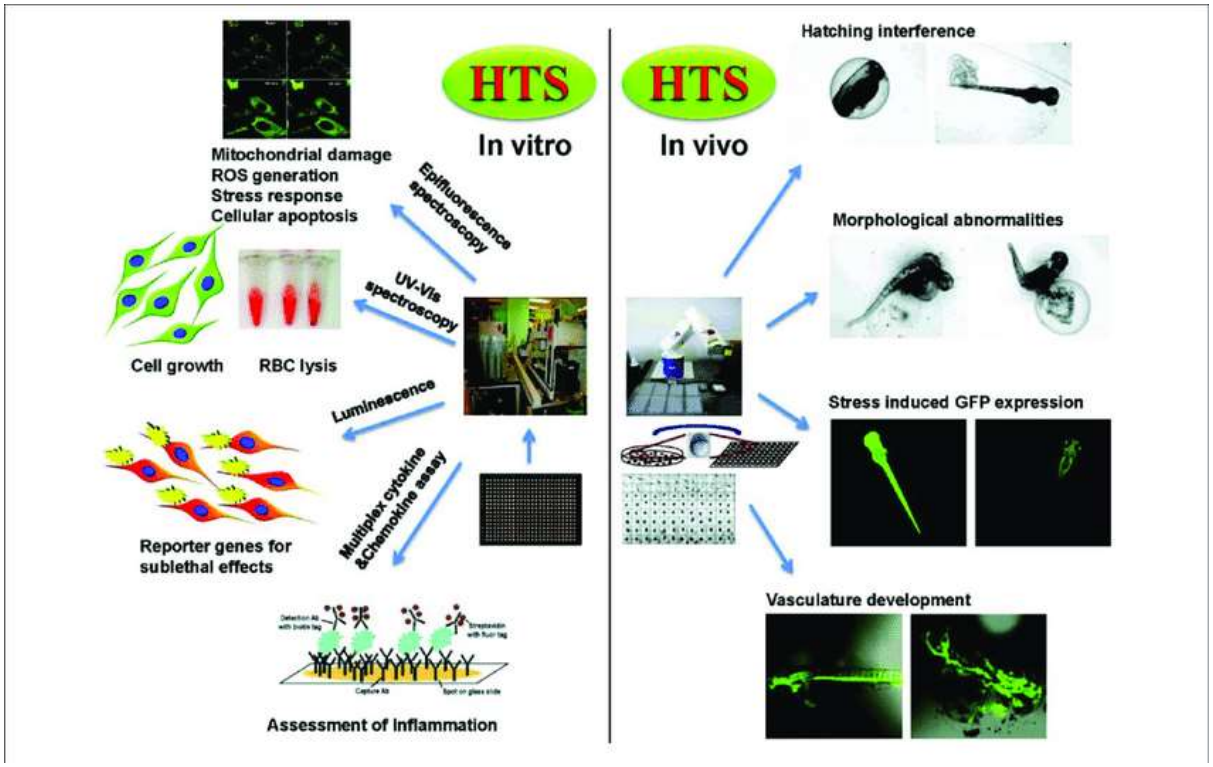
Types.	**Examples**.	**Properties**
Natural polymers	Hyaluronic acid and collagen.	Great biocompatibility; short degradation time; low viscosity
Hydrogels.	Pol (vinyl alcohol) poly (1-vinyl-2-Pyrrolidone). polyacrylamide.	Great biocompatibility; stable transparency, and viscoelastic properties
Transplants and. Implants.	Artificial capsular bodies (foldable capsular vitreous body).	Good mechanical, optical, and biocompatible properties; may cause retinal disorders due to long-term capsule-induced mechanical pressure.

Table- 4 [6] Cell Culture Models of Blood- Brain Barriers

Species.	**Application(s)**
Retinal pigment epithelium	
Primary isolated bovine cells.	Assessment of barrier function.
Primary isolated rat cells.	
Immortalized rat RPE-J cell line	Polarity and functions of the retinal pigment epithelium
Immortalized human cells (ARPE- 19).	Toxicity, gene delivery, and polarity studies
Retinal capillary endothelium.	
Primary isolated bovine retinal capillary. (BRCEC)	Permeability studies
Immortalized rat retinal capillary endothelium.	Barrier properties

Table- 5 [7] Ex Vivo Organotypic Models Used in Ocular Testing.

Name.	**Test method indicator.**	**Testing Objective**	**Validation status.**	**Limitations**
Bovine corneal opacity and. permeability. (BCOP).	Increase in corneal thickness. permeability, and opacity.	Ocular sensitivity and corrosion.	EVCAM statement of. scientific validity for identification of severe irritants and ocular corrosives.	Not as sensitive in distinguishing between mild irritants with standard protocol
Isolated chicken. eye (ICE).	Increase in corneal thickness, permeability, and opacity.	Ocular sensitivity and corrosion	EVCAM statement of scientific validity for. identification of severe irritants and ocular corrosives	Possible limitation for solids
Isolated rabbit. eye (IRE).	Increase in corneal thickness, and opacity	Ocular. sensitivity and corrosion	Further review is. recommended.	Possible limitation for solids.



4. Conclusion

Tissue engineering has developed biologically equivalent replacements which are used for research. Development of in vitro representation of organs for drug toxicity assessment, to study the ocular drug delivery system in more efficient way. The use of invitro platforms has been greatly attributed to obvious cost and ethical advantages over in vivo models. Hence physiologically accurate in vitro models of the eye to assess drug delivery and safety of new ocular therapeutics is necessary. This review summarizes various available cell models, their uses and limitations. This can be helpful for further research in ayurvedic ocular drug delivery system.

Authorship

Each of the identified authors made substantial intellectual contributions to paper design, and bibliographic research

Conflicts of interests

There are no competing interests, according to the authors**.**

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