RESEARCH PAPER

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Ophthalmic Irritation Potential of Propylene Glycol

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Propylene glycol, a new vehicle for ophthalmic use tested here, has proved to be non-toxic to the rabbit eye. There was no serious vision - threatening side effects or a microscopic structural damage to the eye. It was proved to be safe on frequent usage too. All irritation scores recorded being consistently below the "Mariginal Irritant" scope of 65.

WATER for injection has been used as a vehicle for ophthalmic solutions but it is not suitable as a solvent for a wide variety of antibacterial and antifungal agents and their combinations which are insoluble in it. Moreover it is not viscous enough to retain the drug in the eye for adequate time. Though oils are viscous and have been tried they have not received acceptance. For an ophthalmic vehicle to be acceptable it should be viscous, non-irritant, water miscible and it should be a solvent for a variety of drugs. Propylene glycol was considered as a possible candidate for this purpose.

Before any liquid can be used as a vehicle for opthalmic preparation, it has to be thoroughly investigated for its irritation potential. Here a systematic toxicity study was undertaken on this vehicle the potential for permanent damage any vehicle may exhibit, accentuates the necessity for an animal model that enables extrapolation of the data to man. The rabbit is the animal of choice[1] at the present time for ocular irriation evaluations. It closely resembles the human external eye. However extrapolation must be done with the knowledge that many differences do exist. The rabbit has in fact been shown to be more sensitive to many materials than the human eye. With this background in mind, the rabbit eye was chosen for this study.

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MATERIALS AND METHODS

Materials

1. Propylene glycol obtained from Ranbaxy Laboratories Limited, having a refractive index of 1.4320 to 1.4330, with a Wt/ml at 20° C of 1.0350 to 1.0370 g and boiling range of 186 - 188° was used in the present study. New Zealand white albino rabbits of either sex, weighing about 2 kg were employed in this investigation.

Evaluation of irritation potential of propylene flycol

For evauation of the irritation potential of propylene glycol the following methodology was adopted[2]. Batches of New Zealand white albino rabbits were chosen. All eyes were found to be normal externally on slit lamp examination under cobalt blue illumination.

Batches of six rabbits were used as a time for each study. One drop of propylene glycol was instilled into the conjuctival sac. The lower lid was gently pulled away to form a cup and propylene glycol was then instilled and the lids were held together for a second. The contralateral eye served as a control. The eyes were examined and graded after 24, 48 and 72 hours and on day 7 after instillation. Each

examination included a study with fluorescein 2% topical drops (excess was washed with sterile water). Fundus examination with direct opthalmoscope was perfomed everyday. Slit lamp observations were scored as follows:

Corneal damage

Corneal damage (Edema thickeness), Flurescein (punctate staining and confluent staining) and Corneal Vascularization Scaring of pugment migration. (Each)

	Scorig
0 < Area < 1/4	1
1/4 < Area < 1/2	2
1/2 < Area < 3/4	3
3/4 < Area < 1	4

Intensity

Epithelial edema plus slight stromal edema	1
One and a half times normal thickness	2
Two times normal thickness	3
Cornea entirely opaque	4
Corneal Perforation	4
Corneal total =	20

Anterior chamber

Cells

A few	1
Moderate number	2
Many	3

Flare and Hyperemia of Iris (Each)

Slight	1
Moderate	2
marked	3

Pupillary light reflex

Sluggish	1
Absent	2
Iris total =	11

Lids and Conjuctival Damage

Hyperemea, Chemosis, Ulceration, Scarring (Each)

Slight	1
Moderate	2
Marked	3

Staining

Slight (1/3)	1
Moderate (1/3-2/3)	2
Extensive (2/3-3/3)	3
Lid and Conjuctival Total =	15

Bayard and Hehir (Gilman, 1982) considered cornea and iris injury to be morew relevant to the over all irritation potential and proposed weighing the daily scores by using a multiplier of 15 for corneal damage score, and a multiplier of 5 for iris scores and a multiplier of 2 and lids and conjuctival damage scores.

The total score is further weighed as shown below;

Total score = Day 1 scores + Day 2 scores + Day 3 scores + Day 7 scores Final scores were evaluated using the following scale.

Severe iritant : 326 - 550
Strong irritant : 201 - 325
Moderate irritant : 66 - 200
Marginal irritant : 65

Based on the above guidelines, evaluation of the irritation potential was carried out.

In the first part of the study, 1 drop of propylene glycol was instilled into the left eye of all six rabbits (The right eye served as a control) and the eyes examined on days 1,2,3 and 7. In the second part of the study, 1 drop of the propylene glycol was

Table - 1: Scores recored when examined on days 1,2,3 and 7 after 2 drop of propylene glycol was instilled into the left eye of all six rabbits.

RABBIT NO.		DAY 1	DAY 2	DAY 3	Day 7	Total Score
1.	Conjuctival scores	2x2=4				
	Corneal scores	1x15=15				19
	Day total	19				
2.	Conjuctival scores	1x2=2				
	Corneal scores					2
	Day total	2				
3.	Conjuctival scores	1x2=2	1x2=2			
	Corneal scores	1x15=15				19
	Day total	17	2			
4.	Conjuctival scores	2x2=4	1x2=2			
	Corneal scores					6
	Day total	4	2			
5.	Conjuctival scores	1x2=2				
	Corneal scores					2
	Day total12					
6.	Conjuctival scores	1x2=2	1x2=2			
	Corneal scores	1x15=15				19
	Day total	17	2			

Note: Conjuctival scores were all for hyperemia - slight or moderate. Corneal scores were all for punctate staining of cornea involving less than one quarter are.
Iritis was absent in all the eyes.
Fundus was normal in all the eyes.

instilled into the left eye of all the six rabbits once every 24 hours for 3 consecutive days and the eyes examined on days 1,2,3 and 7 (right eye served as a control).

RESULTS AND DISCUSSIONS

When one drop of propylene glycol was instilled and the rabbit eyes examined thereafter on days 1,2,3 and 7 **(Table -1)**, the only consistent finding was the slight to moderate conjuctival hyperemia seen on day 1 in all the rabbits this hyperemia quickly resoved in 24 hours. There rabbits have shown every minimal supericial punctate staining involving far less than one quarter of the cornea. This too resolved in 24 hours. There were no other anterior or posterior segment findings. The maximum score recorded was 19 which is well below the "Marginal Irritant" score of 65.

The results were almost the same when 1 drop of propylene glycol was instilled every 24 hours for 3 days and examined on days 1,2,3 and 7 **(Table -2)**. The slight hyperemia had lasted in 2 rabbits upto day 3. One rabbit showed punctate superficial staining of less than one quarter of the cornea which

Table - 2: Scores recorded after one drop of propylene glycol was instilled into the left eye of all the 6 rabbits once every 24 hours for 3 consecutive days.

RABBIT NO		DAY 1	DAY 2	DAY 3	DAY 7	Total Score
1.	Conjunctival scores	1x2=2	1x2=2			
	Corneal scores	1x15=15				19
	Day total	17	2			
2.	Conjunctival scores	2x2=4	1x2=2	1x2=2		
	Corneal scores	1x15=15	1x15=15			38
	Day total	19	17	2		
3.	Conjunctival scores	2x2=4	1x2=2			
	Corneal scores	1x15=15				21
	Day total	19	2			
4.	Cojunctival scores	1x2=2				
	Corneal scores	1x15=15				17
	Day total	17				
5.	Conjunctival scores	2x2=4	1x2=2			
	Corneal scores					6
	Day total	4	2			
6.	Conjunctival scores	1x2=2	1x2=2	1x2=2		
	Corneal scores	1x15=15				21
	Day total	17	2	2		

Note: Conjunctival scores were all for hyperemia - slight or moderate Corneal scores were all for punctate staining involving less than one quarter area of cornea.
Iritis was not present in any eye.

resolved on day 3. The maximum score recorded was 38 which is again below the "Marginal Irritant" score of 65.

The present study has opened portals for using propylene glycol, hither to unused as a vehicle in ophthalmic drops, for investigating different drug combinations for effective therapy in ophthalmology.

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