

# A SCINTIGRAPHIC INVESTIGATION OF THE PRECORNEAL RESIDENCE TIME OF TS POLYSACCHARIDE FORMULATIONS IN MILD TO MODERATE KCS PATIENTS

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## INTRODUCTION

Repair and restoration of the tearfilm in conditions involving mucin-disorders such as *Keratoconjunctivitis sicca* (KCS) requires the administration of hydrophilic polymers which are able to resist desiccation and provide lubrication for lid and eye movement. The most effective preparations developed to date have been those based on hyaluronic acid or oily bases, although the latter may cause blurring of vision. Formulations based on other biopolymers such as xanthan gums and alginates have also been introduced. Recently, a polymer derived from the tamarind seed (TS-Polysaccharide) has been investigated as an ophthalmic vehicle. Solutions of the polymer have high viscosity and mucoadhesive properties and have been shown to be an effective tear substitute in a rabbit dry eye model<sup>1</sup>.

## METHODS

### Design

Single-centre, randomised, analyst-blind, four-way crossover study.

### Subjects

12 (four females, 8 males) diagnosed mild to moderate KCS patients age 39 to 62 (mean 51.1 +/- 8.0).

Diagnosis was made by questionnaire and ophthalmological examination.

### Investigational Products

The following formulations were supplied by Farmigea S.p.A.

- 0.5% w/v TS-polysaccharide (0.5% TSP)
- 1.0% w/v TS-polysaccharide (1% TSP)
- 2.0% w/v TS-polysaccharide (2% TSP)
- 0.4% w/v hyaluronic acid (HA)

Formulations were aseptically labelled on the day of dosing with <sup>99m</sup>Tc-DTPA (1MBq per 25µl dose). The labelling had no significant effect on the rheological properties of the formulations.

### Dosing

Subjects were dosed according to a randomisation schedule. A single drop (25 µl) of the appropriate test preparation was instilled into one eye using a calibrated positive displacement pipette. Each study arm was separated by a seven-day washout period.

### Imaging Schedule

Subjects were seated at an ophthalmic table positioned 75mm from a low energy high resolution collimator with chin and forehead supported. A dynamic view was recorded for 10 minutes post dosing. Subsequently static views were collected every 5 minutes for a period of 30 minutes then every 15 minutes until 2 hours post dose.

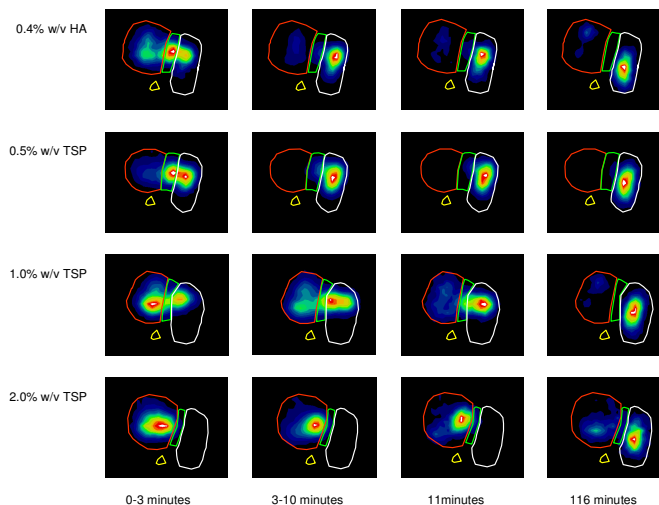


Figure 1 Images from a single subject showing the distribution of radiolabelled ophthalmic formulations at 0-3 minutes (summed dynamic images), 3-10 minutes (summed dynamic images), 11 minutes (static image) and 116 minutes (static image). The corneal ROI is shown in red, inner canthus in green, lacrimal duct in white and background in yellow

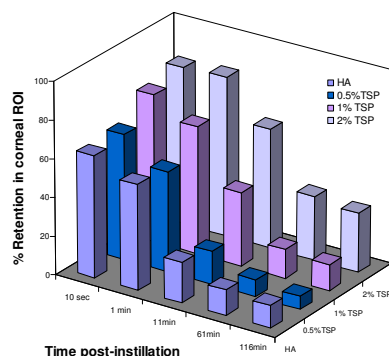


Figure 2  
Graph of mean % retention in corneal ROI

Formulation	AUC <sub>0-600</sub>	SD	AUC <sub>Total</sub>	SD
0.5% TSP	20330	10870	78464	71911
1.0% TSP	35071	13850	140893	91716
2.0% TSP	47941	9173	267820	124860
0.4% HA	22219	11681	103666	121002

Figure 3  
AUC<sub>0-600</sub> and AUC<sub>Total</sub>  
(mean +/- standard deviation, %s)

## ANALYSIS

Images were analysed using the WebLink<sup>®</sup> image analysis program. The dynamic images were summed to produce an overall picture of the label distribution. Regions of interest (ROI) were constructed for each eye, including the cornea, inner canthus, lacrimal duct and background (Figure 1). All counts were background and decay-corrected to express clearance and normalised to count rate at the time of instillation. Any hot spots due to contamination of eyelashes or surrounding skin were determined by construction of additional ROI and corrected for in the final analysis. T<sub>50</sub>, T<sub>20</sub> and AUC<sub>0-600</sub> and AUC<sub>Total</sub> were calculated using a validated Microsoft Excel spreadsheet.

## RESULTS

All materials were retained on the cornea for a prolonged period with material still present on the corneal surface at approximately 2 hours post-dose (Figure 1). The greatest retention was observed with the higher percentage concentrations of TS-polysaccharide (2.0 and 1.0%). Both 2.0% and 1.0% exhibited greater retention than 0.4% hyaluronic acid. The 0.5% formulation had a comparable profile to the hyaluronic acid solution (Figure 2).

The relative proportions of the total label remaining on the corneal surface at the end of the dynamic acquisition (mean ± standard deviation) were 66.9 ± 18.2% for 2.0% and 42.1 ± 22.9% for 1.0% compared with 20.2 ± 16.4% for the 0.5% and 22.2 ± 20.0% for the hyaluronic acid formulation. These differences are reflected in the values for AUC<sub>0-600</sub> and AUC<sub>Total</sub> (Figure 3).

The pattern of retention strongly suggests a tear-structuring effect of the TS polysaccharide. All compounds were well tolerated and no reflex tearing was noted.

## CONCLUSION

TS polysaccharide formulations are well tolerated and have greater retention on the corneal surface than hyaluronic acid.

## REFERENCES

1. Burglasi S. *et al* (1999) *Ophthalmic Research* **31**: 229-235

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