## CLINICAL INSIGHTS BASED IN CURRENT RESEARCH

## Article Review: Rheological behavior of commercial artificial tear solutions

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Arshinoff, S., Hofmann, I. and Nae, H., 2021. Rheological behavior of commercial artificial tear solutions. Journal of Cataract & Refractive Surgery, 47(5), pp.649-654.

The rheological behaviour of a material or liquid is an unfamiliar topic for most clinicians, since it refers to the manner in which that material or liquid deforms or flows. It can be used to describe how cement can flow, or how paint can spread on a surface. We encounter rheological behaviour in materials and liquids every day, but it typically goes unnoticed, unless we are trying to get ketchup to flow out of a bottle!

Fluid mechanics, for that is what is being described, can also be labelled as being Newtonian or non-Newtonian. In a fluid with Newtonian characteristics, the response of the fluid to an external force is linear – as the external force applied increases, the response of the fluid remains constant. Water or air show Newtonian characteristics. Another way of describing this is to say that the viscosity of the fluid remains constant, with viscosity describing the resistance of a fluid to deformation. In common language we might say that oil is thicker (more viscous) than water. Thus, in a Newtonian fluid, the viscosity remains constant even as the external force applied increases or decreases.

In contrast, a non-Newtonian fluid will respond differently as the external force applied increases, with it becoming more or less viscous. Non-Newtonian fluids are very common – ketchup is a good example! The ketchup is gellike initially, but as a force is applied, it transitions into a liquid, producing that unexpected sudden rush of sauce onto the plate!

As clinicians we have a keen interest in rheology, since the rheological behaviour of the ocular tear film is crucial in how the tear film provides stable vision, as well as lubricates the movement of the eyelids. While the eyelids are open, we need a stable tear film that does not flow, but is gel-like and resists deformation. However, when the eyelids are moving, we need a tear film that does not resist deformation and thus slow the eyelid's movement over the ocular surface. In other words, the tear film must act as a non-Newtonian fluid. Non-Newtonian responses in the tear film are dependent on its composition. As tear film composition alters in dry eye disease, so does the non-Newtonian response of the tear film. It is thought that this altered response has a clinical consequence in increased signs of friction on the conjunctiva – resulting in clinical conditions such as lid wiper epitheliopathy (LWE) and lid parallel conjunctival folds (LIPCOF), and in increased symptoms of discomfort.

For clinicians treating dry eye, an artificial tear solution must be capable of mimicking the rheological performance of the healthy tear film to enable a rebalancing of the abnormal tear. Clinicians, patients and designers of artificial tear solutions thus have a keen interest in understanding how a solution performs under deforming stress. This

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article by Arshinoff et al. seeks to answer some of those questions by examining a selection of commercially available artificial tear solutions with the specific aim of analysing their rheological behaviour. Their aim was to discover whether a solution's Newtonian or non-Newtonian response could be used as a predictor of a its clinical potential, and thus be useful as a tool in the design of future artificial tears.

The study is a lab-based approach that uses a specialised instrument to measure the rheological performance of each artificial tear solution. The results produced three main groupings: solutions with a strong non-Newtonian response, solutions with a moderate non-Newtonian response, and solutions with a Newtonian response. These responses were determined by the composition of the solution. Interestingly, solutions with similar chemical composition could perform differently due to the precise chemical formation of the principal components. For example, hyaluronan is a key component of non-Newtonian fluids, but the length of the molecule used (its molecular weight) has a big effect. A longer molecular chain produces greater interactions with other solution components and decreases its non-Newtonian performance. The authors used this example to emphasise that a simple reading of the solution ingredients is not a sufficient guide to judge its rheological performance.

Broadly, the authors suggest that a solution with a higher non-Newtonian rheological response should perform better for most patients, since it is more likely to prolong the solution residence time, and thus the beneficial effects of solution instillation. The authors report that all of the solutions classified as non-Newtonian by the authors met this standard. The authors make no comment on the Newtonian solutions, but we may conclude that the solutions are able to assist the tear film by increasing overall tear volume, even if not directly boosting the tear film by adding non-Newtonian components.

The authors note that their results reflect the performance of these solutions under one set of laboratory conditions and not the on-eye performance. There may be a difference between these results and how a solution might perform on any individual patient. Thus, the Newtonian solution may still produce a rheological benefit to a patient (undetected in this study) by modifying the overall composition and balance of the tear film to improve the tear film rheological performance. In contrast, a non-Newtonian solution may have an unwanted effect of producing excessive viscosity in the tear film that prevents smooth tear film spreading during the 'quiet phase' when the eyelid is no longer moving, leading to blurred or inconsistent vision between blinks. While the results of this paper are of keen interest to solution manufacturers, they are also informative for clinicians in revealing some of the secrets of how these solutions are prepared, and how they perform in rheological terms. They may also guide a clinician in choosing an artificial tear solution for their patient. However, further work is needed to link these laboratory results with the on-eye performance of the solutions tested.