Simerdip Kaur takes a look at the latest ophthalmology-related news stories and asks which are scientific reality and which are 'fake news'.

Headline:
"My cataracts have been dissolved by eye drops!"

I'm sure some of us have had patients enquire about 'cataract-dissolving' drops but is it really true? And if so, how does it work?

A popular eye drop 'Can-C' containing N-alpha-acetylcarnosine (NAC) claims to reduce, reverse and slow the development of senile cataract. It was developed and is patented by Professor Babizhayev, a bio-physicist and Executive Director of Innovative Vision Products (IVP) [1]. In a separate book by Marios Kyriazis – an anti-aging physician expert, NAC is hailed as "The Cataract Cure" and is also the title of his book that briefly explains the miracle of NAC in relation to research by Babizhayev [2]. The author explains that NAC is a free radical scavenger and blocker of cross-linking, a process whereby glycated proteins bind with other proteins and form large insoluble amounts of damaged protein that can accumulate in and disrupt the natural arrangement of the lens crystallin fibres. NAC is closely related in its molecular structure to its active form L-carnosine that it transforms to on entering the lens. It is able to do so as NAC is resistant to degradation within the aqueous humour by the enzyme carnosinase [2]. IVP claims to produce a unique purified formula of NAC through a specific (cyclic guanosine monophosphate) cGMP process in Japan which is then incorporated in its 'Can-C' drop which contains 1% of NAC, de-ionised water, 1% glycerine and 0.3% carboxymethylcellulose which act as lubricants and stabilisers, 0.3% benzyl alcohol as preservative and potassium bicarbonate and potassium borate as buffering agents [3]. The drops are available online, two 15ml vials cost £19.70 on Amazon Prime. The recommended dose is one to two drops twice a day for four to six months, after which the user is expected to taper the regime to two drops once a day on the assumption that they have noticed a difference [4].

Babizhayev has conducted the majority of the research on the use of NAC in animals and humans. In particular, his study from 2002 aimed to test the efficacy of NAC in the treatment of cataracts in humans via a randomised, placebo-controlled trial, that was carried out in 49 subjects of which there were 76 eyes affected by cataracts [5]. Their outcome measures were best corrected visual acuity (BCVA), degree of cataract via stereocinematographic slit-images and retro-illumination, as well as degree of glare sensitivity. Their results suggested that patients who were treated with the NAC drops had shown improvement across the board compared to the patients who did not receive the treatment. Nevertheless, this study can be criticised in several ways. Firstly, there was no mention of blinding of the investigators in the methodology or analysis of results. Secondly, the follow-up time is inconsistent as some participants were followed up to six months whilst others up to two years. Additionally, not everyone in the control group received placebo as some of them received no treatment. There is also the glaring conflict of interest as the author is linked to the company that produces the NAC drops.

My disappointment seemed to be echoed by a Cochrane review by Dubois and Bastawrous in 2017 on the effectiveness of NAC drops to prevent or reverse age-related cataract [6]. Unsurprisingly, the authors only managed to identify two potentially eligible studies, conducted by none other than by Babizhayev, in 2002 and 2004. However, both studies remain unclassified as there was insufficient information on their design and methodology. It is thus reasonable to inform your patient that whilst there is seemingly no harm in trying NAC-containing drops to 'dissolve' their cataracts, there is no research evidence to prove that it is effective.

NAC isn't the only compound implicated as a potential agent to reverse and 'dissolve' cataracts, as shown by Zhao et al. in 2015 [7]. They discovered mutations in lanosterol synthase (LSS) that contributed to congenital cataracts in three children from a consanguineous Caucasian family. LSS synthesises lanosterol which is naturally occurring in the lens as an amphipathic molecule, i.e. it is both hydrophilic and hydrophobic. In Zhao's in vitro study, lens tissues from rabbits were immersed in solution of lanosterol for six days in the dark at room temperature; whilst in the in vivo study, dogs' eyes received intravitreal injections of lanosterol loaded nanoparticles as well as topical lanosterol drops and the outcomes were measured six weeks later. The degree of cataract assessed by lens clarity before and after the treatment periods was assessed by blinded examiners using an opacification grading system. They found a statistically significant reduction in cataract severity and improvement in lens clarity post-treatment in both studies. They concluded that lanosterol inhibits lens protein aggregation by coating the hydrophobic core areas of large protein aggregates within the lens, thus rendering them water-soluble which improves their clarity.

Shanmugam et al. attempted to replicate Zhao's success in human lenses by extracting 40 human senile cataractous nuclei via small incision manual cataract surgery and randomly immersing half of them in a lanosterol solution of the exact concentration as in the rabbit study, and the other half in a control solution for six days [8]. Unfortunately they discovered a worsening degree of cataract in both the treatment and control group as graded by masked observers. As there was no lens capsule or cortex in Shanmugam's study due to their nuclei extraction method they argue that lanoserol should have easier access to the lens fibres, however, this was not the case. They postulated several reasons for this, one of which could be due to difference in concentration of lanosterol needed for reversal of protein aggregation in human lenses. Also, other compounds besides lanosterol could be contributing towards cataract formation.

And so it appears that, for the time being, cataract surgery remains the only option for improving vision in patients with lens opacification. It is not only the most common operation performed in the NHS but also one of the oldest known surgical procedures that has evolved from couching to phacoemulsification.

References

1. Innovative Vision Products, Inc. http://www.innovative-vision-products.com
2. Kyriazis M. *The cataract cure. The Russian eye-drop breakthrough: The story of N-acetylcarnosine.* iUniverse; New York: 2005.
3. Nacetylcarnosine.com http://www.nacetylcarnosine.com
4. Can-C Eyedrops. Helping to Reverse Senile Cataract. http://www.can-c.net
5. Babizhayev MA, Deyev AI, Yermakova VN, et al. Efficacy of N-Acetylcarnosine in the Treatment of Cataracts. *Drugs in R&D* 2002;**3(2)**:87-103.
6. Dubois VD, Bastawrous A. N-acetylcarnosine (NAC) drops for age-related cataract. *Cochrane Database Syst Rev* 2017;**28(2)**:CD009493.
7. Zhao L, Chen XJ, Zhu J, et al. Lanosterol reverses protein aggregation in cataracts. *Nature* 2015;**523(7562)**:607-11.
8. Shanmugam PM, Barigali A, Kadaskar J, et al. Effect of lanosterol on human cataract nucleus. *Indian J Ophthalmol* 2015;**63**:888-90.

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