

A high standard of delivery

ADS takes skin delivery to a new level of efficacy and safety, opening up exciting possibilities for 'in and out' treatments using a common core active molecule, say Liliana Todorinova & Helena Larsson

When used in beauty products, nanotechnology-based delivery systems address three key issues.

Firstly, they aim to increase the bioavailability of their encapsulated active molecules en route to the target site. This optimises efficacy levels across the relevant body barriers – the skin for topical application and the digestive tract for oral application.

Secondly, consumer safety is paramount. All nano-based actives should be based on safe, biodegradable materials and should also limit the efficacy to a specific organ, tissue or even type of cell.

Finally, nanotechnology-based delivery systems should simplify the formulations of finished products. This incorporates aspects such as stability with a range of temperatures, pHs and common ingredients, reduced colour and smell, and extended shelf-life. These factors help in retaining a formulation's active molecule content, which in turn helps to avoid customer disappointment. Cosmetics that use antioxidant plant extracts often fall short of their claims, for example because they require special packaging, have shorter shelf-lives and an overall limited degree of marketability.

Nanotech engineered delivery systems should improve the stability, safety and bioavailability of an active ingredient to the point where it can be used in a wide variety of oral and topical applications. Reaching this level allows many 'in and out' treatments to be offered from a common core active molecule.

MULTIPLE BENEFITS

As a new generation of nano delivery systems, ADS satisfies all of the above requirements. It gives finely targeted delivery to sites currently unreachable with other methods and offers a superior level of safety plus an outstanding degree of encapsulated active stability.

A nano-size liposome of amino phospholipids, ADS is incorporated with patented Nano Active Receptors (NARs) from fenugreek. When embedded in a membrane of other bio-active ingredients, it then plays the role of a guiding device to deliver the encapsulated active molecules to a pre-defined target site. This allows for targeted, innovative and controlled release of active compounds which will only reach the skin, regardless of whether the active is administered orally or topically.

This new delivery system offers the following benefits:

- Made from 100% vegetable ingredients
- Sustained delivery over a long period of time
- Targeted delivery, in time as well as space
- Lower required dosage of the administered actives – avoiding the risk of overdose
- Protection against external aggression and heat resistance
- High concentration of actives

ADS can be tailored to fit specific needs. Modifying the composition and size of the nano carrier affects the speeds of degradation and content delivery. It is also possible to increase the targeting accuracy by changing its composition or electrical charge, or by adding receptors or adhesion factors to its outer surface.

Thanks to its outstanding stability and safety, it allows the same active ingredients to be delivered both orally and topically, increasing its marketable potential.

POMEGRANATE ANTIOXIDANTS

This ability to deliver active molecules to specific skin sites has been demonstrated with Viqua, a concentrate of pomegranate antioxidants encapsulated through the ADS nanotechnology.

Numerous studies have shown the potential whitening and anti-ageing benefits of pomegranate antioxidants for the skin.

However, finished products containing pomegranate extracts have so far been limited in their effects due to a lack of stability in one of the fruit's main active molecules, punicalagin.

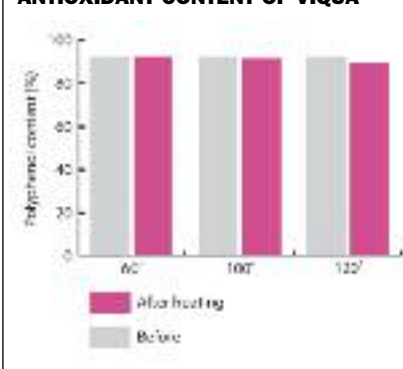
Viqua is a new type of nano-engineered antioxidant that is made up of a pomegranate extract titrated in 40% punicalagins and then encapsulated by ADS nanotechnology. The encapsulating carrier uses phospholipids which have been extracted from pomegranate seed oil, making Viqua a 100% pomegranate extract product.

Dramatically improved stability of the pomegranate antioxidants is the first benefit of the encapsulation process. When heated to 100°C for one hour, the antioxidant content of Viqua now remains almost unchanged (figure 1). Additional tests showed the ingredient to be completely safe in oral as well as topical applications.

In vitro the encapsulated pomegranate extract shows a dose-dependent, SOD-like antioxidant activity which is superior to most common antioxidant plant extracts. Additionally, Viqua demonstrated the ability to inhibit the destructive action of



FIGURE 1
ANTIOXIDANT CONTENT OF VIQUA



the skin enzymes collagenase and elastase, thus potentially protecting the skin from the effects of premature ageing.

The real breakthrough of Viqua however is its ability to specifically transport the pomegranate antioxidants into the skin cells' mitochondria, believed to be only possible through ADS nanotechnology.

MITOCHONDRIA PENETRATION

Viqua can be shown to penetrate skin cells intact. In an in-vitro test, human 3T3-L1 adipocytes were cultured for three hours with Viqua, into which had previously been incorporated a fluorescent red marker. After incubation, fluorescent microscope pictures revealed that Viqua is specifically located inside the adipocytes, and more specifically in the zones surrounding the lipid droplets, known to be extremely abundant in mitochondria (figure 2).

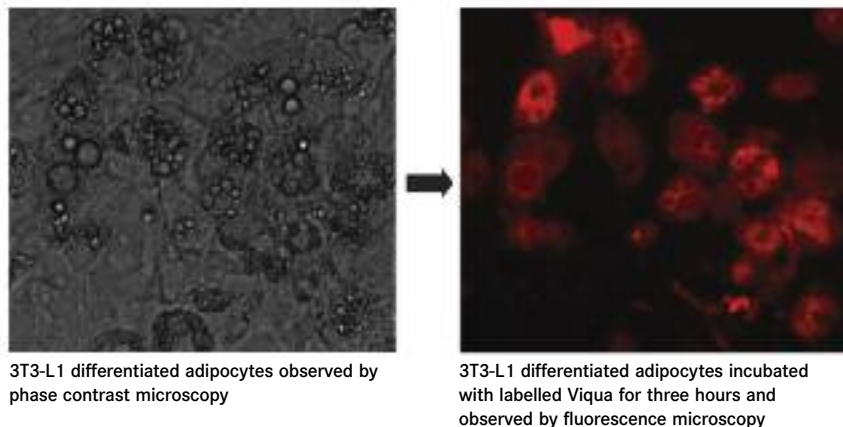
Viqua is not only located inside the cells either, but also performs its antioxidant action from there. In a second test, adipocytes (both cultured with Viqua and not) were subjected to elevated oxidative stress, created by the addition of H₂O₂.

Viqua cultured adipocytes show a dose-dependant ability to reduce oxidative stress (figure 3), thus proving that the ADS powered antioxidants which are located inside the cells are active.

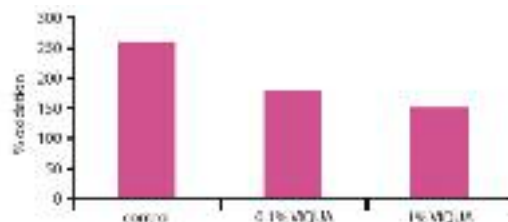
A further study demonstrated that Viqua specifically targets the cell mitochondria. In this study, the same adipocytes which were previously cultured with red fluorescent Viqua were also marked by a specific MitoTracker Green FM probe stained in fluorescent green; this compound is known to accumulate exclusively inside cell mitochondria. As a result, the MitoTracker's position on a microscope picture shows the exact location of the mitochondria inside the observed cells. Figure 4 shows microscope pictures of the same adipocytes: on the upper left is a contrast phase microscopy image without fluorescence; on the bottom left is a fluorescence image stained green for the MitoTracker; on the upper right is an image which has been stained red for Viqua presence; on the bottom right is an image which has been superimposed with both the MitoTracker and Viqua fluorescence images. As can be seen, the green and the red fluorescence appears on the same sites inside the cell. It can therefore be concluded that Viqua is located at the same spots as the MitoTracker – ie inside the cell mitochondria.

As the main site of free radical production, and origin of the cell's oxidative stress, the mitochondrion is a key target for any antioxidant treatment. By encapsulating

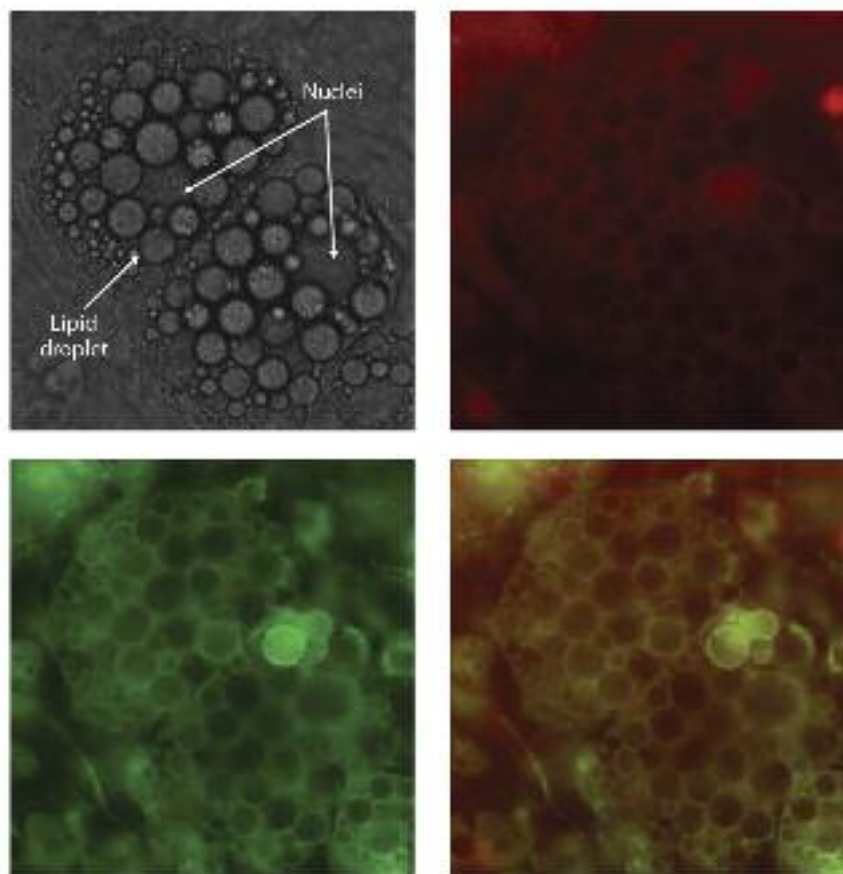
**FIGURE 2
LOCATION OF VIQUA IN THE ADIPOCYTES**



**FIGURE 3
ABILITY TO
REDUCE
OXIDATIVE
STRESS**



**FIGURE 4
VIQUA SPECIFICALLY TARGETS THE CELL MITOCHONDRIA**



pomegranate extracted antioxidants with ADS nanotechnology, Viqua is expected to specifically target the mitochondria of skin cells and perform antioxidant action from inside them, resulting in considerable benefits for the skin.

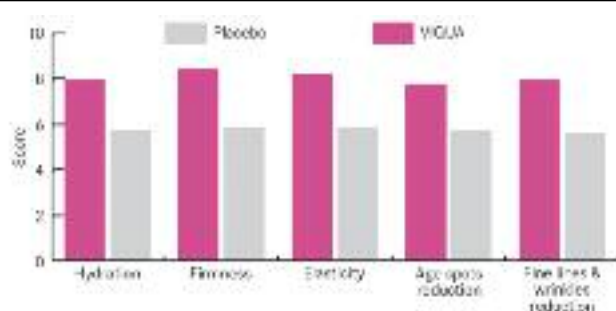
INGESTION CLINICAL STUDY

A double blind, placebo controlled clinical study on 30 volunteers with orally administered Viqua demonstrated its benefits in-vivo:

- Hydration rose significantly (40%), whereas the placebo group saw a decrease (-0.3%). The water content of the skin's upper layers particularly improved with Viqua (51%)
- Skin smoothness improved (27%) – a significant decrease in depth of fine lines and wrinkles was recorded (volume -26%)
- Blood vessel remodelling suggested significant inhibition of inflammation processes
- Skin tone became generally brighter and dark spot/blemish colour attenuated

Volunteer self-assessment results mirrored the product efficacy results proven above. The subjects treated with Viqua always

**FIGURE 5
IN-VIVO
PERFORMANCE
OF VIQUA
ADMINISTERED
ORALLY**



expressed a higher satisfaction score compared with those who were given the placebo

Pomegranates are nature's secret gift to youthful, beautiful looking skin. Viqua follows where nature leads, in this case powered by the innovative ADS nano-delivery system made of pomegranate itself. Viqua concentrates the beautifying essence of pomegranate in its most powerful and bioavailable form. The result is a whitening, anti-ageing and anti-inflammatory beauty product with clinically proven efficacy. Its perfect stability and safety allows use in a diverse range of food and cosmetic applications.

This new generation nano delivery system demonstrates how advancement in nanotechnology exploits the best of nature and science to raise the efficacy and safety of active ingredients to a new level. **cb**

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