CENOMICS

The hottest makeup trend is green: How CRISPR can help the switch to sustainable cosmetics.

> Jon Kratochvil, Vice-President, ERS Genomics.

The global cosmetics industry is worth more than \$500 billion, but relies on ingredients that are unsustainable and cause harm to plant and animal life. Some products are sourced from animals directly and many others cause harm indirectly by persisting and accumulating in the environment.¹

Growing awareness of this problem among consumers has fueled a demand for something different, with green cosmetics emerging as a strong new trend in the beauty industry. In Europe, the natural cosmetics market generated almost €2 billion in revenue in 2020, expected to rise to almost €3 billion by 2025. Globally, this market is predicted to be worth US\$48 billion by 2025.

Consumers are increasingly products with plantderived, 'natural' ingredients and turning away from those containing animal-derived or environmentally damaging components. So what's fueling the hype?

Many cosmetic ingredients are unsustainable Many ingredients commonplace on the labels of cosmetics are animal-derived and environmentally unsustainable.

These include squalene and its derivative squalane, naturally-occurring fatty substances used in a host of products, from moisturizers and sunscreen to lipstick and more. However, much of the squalene in the cosmetic industry comes from sharks² Shark liver oil is a particularly rich source of squalene and global demand is in the region of 2,200 tons³, 90% of which is destined for cosmetics. With 3,000 sharks needed to produce just 1 tonne of squalane⁴, this is a simply unsustainable demand for populations already threatened with overexploitation.

Although plant-based alternatives are available, including squalane derived from olives, rice, and sugar cane, plantbased sources produce significantly lower yields of squalane. This makes it harder to extract and therefore more expensive than shark-derived squalane⁵, leaving many manufacturers little choice if they are to compete on price.



Plant-based ingredients are not a perfect solution for the environment, either. Growing and harvesting any plant has an environmental impact, particularly when it takes place in already vulnerable ecosystems and without restriction. Palm oil is a well-established example of this problem, with the devastating impacts of its harvesting including tropical deforestation and biodiversity loss.





Consumers are becoming increasingly aware of the environmental impacts of palm oil and many strive to avoid it, but what about lesser-known plant-based ingredients making their way into the cosmetics cabinet? **Moroccan argan oil** has become a highly prized, fashionable ingredient in products for hair, skin and nails, quickly propelling it to become the most expensive edible oil in the world. Yet this popularity has also come at great environmental cost to the regions where it is produced.⁶

Bakuchiol is another trendy but potentially unsustainable ingredient. Derived from the Babchi plant native to India, bakuchiol is becoming increasingly popular in skincare products as it is offers similar benefits to retinol but ⁷/₇ without the side effects. As a result natural populations of the Babchi plant, which is already endangered,⁸ are increasingly at risk from indiscriminate and illegal harvesting.

Whatever the origin, intensive processing is generally required to extract precious biomolecules from their source, which creates its own environmental impact and comes at a cost to the consumer.

In a world where consumers are increasingly savvy about the sources of ingredients, the cosmetics industry clearly cannot continue to rely on unsustainable and environmentally harmful ingredients, even though they may be labeled as 'natural'. So, what's the alternative?

CRISPR-ing the cosmetics cabinet

Instead of relying on nature to produce the compounds and quantities required by the global beauty industry, geneediting technology can reduce demand on precious and limited natural resources.

Microbes, including yeast, algae, fungi and bacteria, are capable of producing a range of biomolecules that form the basis of many cosmetics ingredients. These include terpenoids – the precursors of squalene – as well as fatty acids, enzymes, peptides, vitamins and pigments.

Genetic engineering provides the opportunity to fine-tune these existing metabolic pathways, or create entirely novel ones, to make biomolecule production more efficient.

CRISPR-Cas9, a highly precise gene-editing technology, sidesteps the shortcomings of its forerunners by being able to repress or activate existing genes within an organism, or insert new ones, at highly precise locations using a simple design scheme. In this way, CRISPR-Cas9 can be used to engineer microbes to make nature-based cosmetic ingredients using standard biotechnology facilities.

The possibilities CRISPR offers the cosmetics industry are endless. For example, Swiss biotech Evolva is using CRISPR to develop nature-based flavors, fragrances and other cosmetics ingredients.

Compounds already being produced by the company include nootkatone, a citrus compound found in grapefruit peel. Nootkatone is used in perfumes to create a fresh, clean scent, but is notoriously expensive due to the small quantities found in nature and the costs of extraction. Evolva's version though, produced by fermentation with genetically engineered yeast, is sustainable, cost-effective and of consistent quality. Elsewhere, CRISPR-Cas9 is already being used to modify terpenoid synthesis pathways in microbes to lead to overproduction of squalene, creating a sustainable, scalable source that does not involve harm to animals or inefficient crop processing.

Several biotech companies have also set to work using the latest advances in CRISPR gene editing to successfully generate a microbial palm oil alternative using various strains of yeast.

Opportunties for enterprising biotechs

CRISPR is set to revolutionize how the cosmetic industry sources its ingredients. Although synthetic alternatives currently remain more expensive than their naturally derived counterparts, it is likely that consumer pressure – combined with legislative changes and application of innovative technologies like CRISPR – will force a shift in the market.



Crucially though, nothing can be commercialized without securing a license for the use of CRISPR technology. ERS Genomics holds the rights to over 100 patents worldwide covering use of CRISPR/Cas9 in bacteria, plants and animals, and is therefore likely to be the first stop for enterprising biotechnology firms looking to capture a slice of the growing market for nature-identical synthetics.

It's time to end the perception that sticking some plant compounds in beauty products is enough to make them 'green'. CRISPR makes it possible to genuinely address the challenge of sustainability across the global beauty industry and finally turn our cosmetics truly green.

References

- 1. Juliano, C. and Magrini, G. (2017). Cosmetic Ingredients as Emerging Pollutants of Environmental and Health Concern. A Mini-Review. Cosmetics, 4(2), p.11.
- 2. Gohil, N., et al. (2019). Engineering Strategies in Microorganisms for the Enhanced Production of Squalene: Advances, Challenges and Opportunities. Frontiers in Bioengineering and Biotechnology, 7.
- 3. Bloom Association (2012) The hideous price of beauty: An investigation into the market of deep-sea shark liver oil.
- 4. Ciriminna, R., et al. (2014). Catalytic Hydrogenation of Squalene to Squalane. Organic Process Research & Development, 18(9), pp.1110–1115.
- 5. Lozano-Grande, M.A., et al. (2018). Plant Sources, Extraction Methods, and Uses of Squalene. International Journal of Agronomy, 2018, pp.1–13.
- 6. Lybbert, T.J. et al. (2011) Booming markets for Moroccan argan oil appear to benefit some rural households while threatening the endemic argan forest. PNAS 108 (34) 13963-13968.
- 7. Dhaliwal, S. et al. (2018). Prospective, randomized, double-blind assessment of topical bakuchiol and retinol for facial photoageing. British Journal of Dermatology, [online] 180(2), pp.289–296.
- 8. Sehrawat, N., et al. (2014) Psoralea corylifolia L. An endangered medicinal plant with broad spectrum properties. International Journal of Phytomedicines and Related Industries, 6(1):13
- 9. Gupta, P.L., Rajput, M., Oza, T., Trivedi, U. and Sanghvi, G. (2019). Eminence of Microbial Products in Cosmetic Industry. Natural Products and Bioprospecting, 9(4), pp.267–278.
- 10. Park, J., et al. (2018) Heterologous Production of Squalene from Glucose in Engineered Corynebacterium glutamicum Using Multiplex CRISPR Interference and High-Throughput Fermentation. J. Agric. Food Chem. 67; 308–319
- 11. Budiani, A., et al. (2017) Transformation of oil palm calli using CRISPR/Cas9 System: toward genome editing of oil palm. IOP Conf. Ser.: Earth Environ. Sci. 183: 012003