



Ambergris & Clary Sage Oil

A Case Study on Use of Synthetic Biology Replacements



Farmers Affected: 120 Family farms in NC, USA. More in China, Ukraine and France.

Market Value: \$13,6 -18,2 Million US¹

Uses: Fixative & fragrance in perfumes and household products (laundry detergent, fabric softener, dish soaps)

Syn bio Companies: Efflorus, Firmenich, Evolva, Amyris

Hotspots: North Carolina (USA), China, France, Hungary, India

Also Grown In: Crimea, Ukraine and Caucasus regions bordering the Black Sea, Bulgaria, Italy, Morocco, Romania and England.

Cultural Importance: Descriptions of medicinal use of clary sage goes back to the writings of Pliny the Elder (1st century CE). Used widely in perfumes and as a muscatel flavoring for vermouths, wines, and liqueurs. Ambergris is historically one of the most prized scents in perfumery, eg. Chanel N^o 5.

Biodiversity Considerations: The flowering plants have benefits for pollinators, and sage is eaten by many species.

Quality Concerns: Natural ambergris and sage oils have many chemical constituents - syn bio companies usually manufacture only one component of the natural product, not all the molecules present in the natural product.

Patents: Method for producing Sclareol Patent #9267155, # 8617860, #8586328 (Firmenich - Michel Schalk Inventor) US20100311134, EP2569427A1, US8927238, US20150099283, WO2011141855A1

Products: Sclareol, Ambroxide

Brands, Identifiers: Ambrox[®], "Sclareol Bio"

Method: Synthetically engineered yeast and *E. coli* bacteria

Commercialization: Should be on the market in 2016, already produced

Feedstock, Biomass: Sugarcane

Overview

While high-end perfumers may still use the expensive and hard-to-find substance ambergris, which is produced in the intestines of sperm whales, most of the industry now uses a substance known as "ambroxide," synthesized from the compound "sclareol" found in clary sage oil. Ambroxide is used both as a fragrance and as a "fixative" for making scents linger longer in products.

Status: Syn bio ambergris may be available in 2016



R&D

Scale Up

Commercialization

Clary sage, a flowering herb with biodiversity benefits, is commercially grown in North Carolina US, as well as in France, China, Crimea and Ukraine. As at least 3 synthetic biology companies are working towards commercializing a syn bio-derived version of ambergris and/or clary sage oil. Ahead of the pack is flavours and fragrance giant Firmenich, partnered with syn bio company Amyris. Firmenich has announced that their syn bio ambroxide will be commercially available during 2016. Amyris appears to have already shipped 100 tons of syn bio clary sage oil from their Brazilian production facility.



For more information on Synthetic Biology please visit the ETC Group website: www.etcgroup.org/synbio

What is Ambergris / Clary Sage Oil (Sclareol)?

Ambergris is a grey waxy substance, a bile secretion found in the digestive tract of some sperm whales. It has been prized in the fragrance and perfume industry for its delicate odor and fixative properties. Combined with perfume, soaps and detergents, it can intensify and extend scents on such products. Its key chemical constituent is ambroxide. Since natural ambergris is hard to find and hugely expensive, the industry today uses a synthetic version of ambroxide (brand name Ambrox) derived from sclareol - the key compound extracted from clary sage plants (*Salvia sclarea*). Clary sage is a flowering herb originally native to Europe. Small amounts of ambroxide can also be used as a food flavouring ingredient.

Ambergris / Clary Sage as a Natural Product

Natural ambergris is a bile duct secretion from a small percentage of sperm whales and is generally discovered by chance on beaches or floating in the sea - it is a rare and highly valuable find. In 1986 the International Whaling Commission instituted a moratorium on commercial whaling. Although ambergris is not currently harvested directly from whales, many countries also ban its trade as part of the more general ban on the hunting and exploitation of whales.² This has led to supply shortage and price inflation, so perfume makers have turned to substitutes. Clary sage has been commercially cultivated in China, France, Hungary, India, Bulgaria, Italy, Morocco, Romania, England and Ukraine, the Crimean and Caucasus regions bordering the Black Sea. Today however, North Carolina in the USA is the world's largest producer of clary sage oil and sclareol. One North Carolina company, Avoca Inc. - spun out of tobacco giant RJ Reynolds - claims to be the world's primary manufacturer and supplier of sclareol to the fragrance industry, supplying 90% of global clary sage oil. The company has contracted 120 local farmers in 11 counties of North Carolina to grow 25,000 acres of clary sage.³

"It's probably one of the most stable crops that we grow. Clary sage is the backbone of our farming operation and has been for years. It's something we can count on."

Parrish Farms, North Carolina

Farmers get paid according to the pounds of sclareol per load.⁴ Avoca sells about 10% of sclareol for use in fine fragrances, and about 90% enters household products.⁵

Parrish Farms, a family-owned farm corporation in Chowan County, was among the first sage growers in North Carolina. Today, the fourth-generation farm family grows 400 acres of sage, a sizable percentage of their 2,200 acres. They also grow peanuts, cotton, soybeans and wheat, which experience wild price swings. Their sage rotation, however, brings stability, since the price has stayed steady for 15 years.



Parrish says: "It's probably one of the most stable crops that we grow. Clary sage is the backbone of our farming operation and has been for years. It's something we can count on."⁶

The Ukraine and Crimea were previously significant producers of clary sage essential oil. These countries supplied 80% of Russian essential oil production (coriander, clary sage, fennel seeds and others) from 4,000 hectares in two small regions.⁷ Since 2014 however, political instability, turmoil and fighting have disturbed essential oil production in this region, including clary sage.

Biodiversity and Cultural Considerations

Clary sage has long been used medicinally, particularly for improving vision and eye health, and is related to common garden sage. Clary sage oil is sometimes called "Muscatel Oil" because of its use flavouring muscatel wine. As a flowering herb, its production has important biodiversity benefits, supporting pollinators and contributing to natural pest control management.

Promoting bee population and pollinator habitat increases the availability of pollen and nectar resources, and provides secondary benefits to the farms and surrounding landscapes. Contribution to a pollinator habitat enhances overall biodiversity and the ecosystem services it provides, as well as contributing to rural aesthetic.⁸



Additionally, Efflorus, a Canadian start-up mentored and funded by the US-Irish IndieBio Accelerator, is also working on ambergris, musk deer and oud oil. Commercialization dates are unknown.¹¹

Implications and the Future

Synthetic Biology Production

Since natural yields for clary sage may be variable, and manual collection of ambergris is highly unpredictable and expensive, the fragrance industry has been looking for a cheaper and more reliable alternative means for producing ambroxide and sclareol.

Two Swiss firms, Firmenich and Evolva, have separately developed new, synthetic biology organisms that produce sclareol. Scientists working for fragrance giant Firmenich have engineered *E. coli* bacteria to produce sclareol, which can then be turned into ambroxide.⁹ They have also collaborated with syn bio company Amyris, which uses engineered yeast for production. This new version of Ambrox, obtained through synthetic biology, has been scheduled to hit the market in 2016, as announced by Firmenich in a press release dated February 2016.¹⁰ Customs records show that in the first 2 months of 2016 Amyris shipped around 100 tonnes of “Sclareol Bio” from its syn bio biorefinery in Brazil - presumably for sale by Firmenich. In past years, 100 tons was equal to entire global production.

Evolva, which uses yeast as the basis of their synthetic biology process, are also developing a syn bio-derived ambroxide, but no timeline for commercialization has been provided. This work may be part of their partnership with the Japanese fragrance corporation Takasago International.

It is not yet clear how Firmenich’s imminent commercialization of syn bio-derived ambroxide could impact clary sage growers. Firmenich appears to be putting considerable marketing behind the new version of Ambrox, describing it as the result of “green chemistry”; and the recent shipment of 100 tons of sclareol from Amyris makes it clear that significant amounts of bioengineered oil is coming to market to compete with natural sage oil.

Endnotes

- 1 Based on 100 tons x 150-200 US\$/kg
- 2 <https://en.wikipedia.org/wiki/Amergris>
- 3 www.ncfieldfamily.org/farm/the-age-of-sage/
- 4 Joanie Stirs. “The Age of Sage.” *North Carolina Field and Family*. www.ncfieldfamily.org/farm/the-age-of-sage/
- 5 *Ibid.*
- 6 *Ibid.*
- 7 www.elixensamerica.com/our-production
- 8 Stephen D. Wratten, Mark Gillespie, Axel Decourtye, Erix Mader, Nicolas Desneux. Pollinator Habitat Enhancement: Benefits to other ecosystem services. *Agriculture, Ecosystems and Environment*. 159 (2012) 112-122. www.xerces.org/wp-content/uploads/2008/06/2012_AGEE_lr_sec.pdf
- 9 <http://pubs.acs.org/doi/abs/10.1021/ja307404u>
- 10 www.cosmeticsdesign-europe.com/Formulation-Science/Firmenich-announces-large-scale-production-of-Ambrox-using-White-Biotechnology Also: www.wired.co.uk/news/archive/2013-02/28/ambergris
- 11 <https://eu.indiebio.co/efflorus-luxury-fragrances-for-a-sustainable-planet/>