Market Analysis

Saffron is a spice, found in Crocus, which has a distinctive red color. Some research has reported that compounds found in saffron, such as crocin, have potential as neuroprotective, antioxidant, and antitumor agents. These compounds have attracted researchers to proceed and conduct more experiments, especially in the medical area. However, in fulfilling prospective demand of the saffron compounds, found in the crocin pathway, it would take a large amount of land to cultivate the plants needed. Here, we explore the alternative idea of producing crocin through bacteria. In this article, a literature study was used to compare the crocin production between conventional farming and a synthetic biology approach. A study showed the decrement of year wise saffron farming, which could be caused by soil nutrient reduction that was not related to water resource availability (1). Even though the saffron production has fluctuated until 2008, the farming area was decreased significantly. The research also found that there is a declining trend in one of the largest producers, Kashmir, due to urbanization. In order to obtain crocin with high purity, the process of compound extraction is also needed. Currently, the synthetic production of crocin is still uncommon. Regardless, there is a potential for producing crocin through synthetic biology. Thus, iGEM Uppsala 2017 is trying to bypass the saffron farming process for producing crocin. Instead, the crocin production will be executed in *E. coli*. Ideally, this will diminish the extensive use of land for cultivation and reduce unsustainable residue production. To compare the production of crocin in traditional farming to production using synthetic biology, this market analysis was conducted.

Before getting to the actual comparison: the analysis of this study is based on the whole production of crocin – from traditional saffron farming to the extraction of crocin by means of conventional methods. Comparably, we did the analysis of crocin which will be produced from *E. coli*.

Crocin is extracted from the stigma of saffron (*Crocus sativus* L.), a perennial crop which grows in arid to semi-arid lands (2). In the Table A below, the yield, production and cultivated area of saffron are described.

Table A. Yield, production and cultivated area of saffron in 1999 (3)

Country	*Yield (kg ha^{-1})*	*Annual production (tons)*	*Cultivated area (ha)*
Iran*	3.4	160.0	47208
Spain	6.5	29.2	4184
India	2.0	4.8	2440

Greece	5.0	4.3	860
Azerbaijan	4.3	3.7	675
Morocco	2.0	1.0	500
Italy	8.4	0.3	29

*1 ha yields in 10-15 kg dried stigmas

Table B. Conversion of flower stigmas to dry saffron (4,5)

Input	*Output*
1 flower	7 mg dry saffron
150 flowers	1 gr dry saffron
1 kg flower	12 gr dry saffron
110,000 - 170,000 flowers	1 kg dry saffron

As shown in Table B, a freshly picked flower generates an average of 30 mg of fresh saffron or 7 mg when it is dried. To get one gram of dry saffron takes about 150 flowers, a kilogram of flowers can produce 12 g of dried saffron and 1 kg of dry saffron requires 110,000-170,000 flowers (5). Based on these numbers, the production of crocin can be linearly calculated from the saffron production. However, there are several factors which affect the degradation rate of crocin in saffron stigmas. Among of them are humidity, temperature and light irradiation (2). Furthermore Lage & Cantrell (2) mentioned, that this compound degrades naturally in the stigma cells when saffron is in the phase of drying, storage to extraction. According to Straubinger *et al.* (2), the crocin compounds can be found in the stigma after the natural degradation which involves the drying, storage and extraction stages. Therefore, there are some numbers which can be found and known as crocin values (Table C).

Table C. Crocin values generated from cultivation (2)

Crocin Values	*Remark*
0.85–32.4 %	Dry weight
2.9 mg %	Iranian saffron
4.6 mg %	Iranian saffron
5.6 %	Experimental saffron cultivation in Morocco

As can be seen in Table C, the percentage of crocin extraction is quite small. The extraction may reach 32.4 % from dry weight, but, if the production of the compound is only relying on the extraction from the stigma, not only are huge amounts of crocus needed, but also many human resources will be required. Even the biggest producer of saffron (Iran) can only produce up to 160.000 kgs of saffron in 47 ha (4), the optimum production of crocin may need another method to extract it more efficiently. If only focusing on the saffron, the market is very promising. By 2026, the saffron market is expected to have a value of nearly US$ 620 Mn (7). Nevertheless, the production of crocin may have an obstacle if it is produced in the conventional way (farming) or in other words, the production may be more expensive if you extract crocin instead of selling it as saffron.

iGEM Uppsala 2017 is trying to use synthetic biology to expand the crocin pathway, by exploring three different enzymes which can be used to convert the compounds from zeaxanthin up to crocin. If the enzymes can be produced that are required for mass production of the compounds in the crocin pathway it could reduce production costs, specifically, changing the production from farming into synthetic biology through microbes may give huge number of reduction cost. The industrial scale has huge reduction percentage, because not only the cost of reagents, but also reducing the cost of farmland, human resources, instrumentation, insulation and buildings, and some other facilities which are needed. In the market, 1 gram of crocin can be bought for around 250 SEK or 30 US$ (8). Therefore, the compound is quite rare, especially if it is produced from synthetic biology. Additionally, the production may be even faster than using the normal cultivation of saffron.

The are benefits of using synthetic biology to produce the compounds from the crocin pathway, as well as obstacles taking the worldwide perspective of its production into account. Here, we tried to identify the existing market focusing on crocin and comparing with similar products (enzymes from big company).

Table D. The future obstacles and potential benefits in crocin production through synthetic biology

Political	Economic
• GMO policy will be a bit more complicated to deal with	• Overcome the chemically synthesized crocin • Cheaper than normal farming
Socio-cultural	**Technological**
• GMO opinion will rise again • Available job or decreasing the job (for farmer) → this job prevents rural migration	• More invention in bio-product related, packaging, protein purification, and etc. • More in the microbe production

• Urbanisation put stress on the expansion of saffron farming	technology
Environmental	Legal
• Reduce land use and water related to farming • Saffron cultivation is a sustainable usage of arid/marginalized land	• Many researcher will try to patent to the crocin related product

The enzymes for crocin production may lead to a potential market in the future. This can be identified from Porter's five forces (Table E).

Table E. The Porter's Five Forces of Crocin Production

Threat of new entry 1. Several researchers have the same aim using different enzymes. So, there could be someone who is doing similar research. 2. Scaling up to mass production of enzymes might be harder.		
Bargaining power of suppliers 1. The production of crocin through synthetic biology may drive the biotechnology experiment reagents 2. Laboratory and industrial scale for synthetic biology equipment provider might be expanded.	*Rivalry among existing competitors* 1. Big industry in synthetic biology may be interested to take a part producing crocin 2. Because the benefit is so diverse, many existing companies may also start producing similar enzymes.	*Bargaining power of customers* 1. Because the production cost will be cheaper, the cost for selling crocin may be even cheaper than existing crocin in the market. Therefore, the market become more attractive
Threat of substitutes 1. There are several potential enzymes from different pathways to produce crocin with synthetic biology method. 2. The laboratory tools enhancements which may also affect the enzyme production. 3. There is a potential to chemically synthesize the compounds		

If crocin production from synthetic biology can be achieved, there are several aspects which may support a sustainable development perspective. The water consumption of conventional farming may not be needed. Therefore, saffron's cultivation needs may be diminished for crocin production. Not only the needs, but also the land use of saffron farming which can be used for other purposes or focusing on the utilization of saffron.

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