Market Analysis

Crocin is an apocarotenoid, found in Crocus and Gardenia, responsible for the distinctive red color of Saffron. Some research has reported that crocin has potentials as neuroprotective, antioxidant, anticancer and antitumor. These compounds have attracted researchers to proceed and conduct more experiment, especially in the medical area. However, in fulfilling prospective demand of the saffron compound, specifically crocin, it takes a large amount of land to cultivate the plants needed. Here, we try to give the alternative idea for producing crocin through bacteria. In this article, a literature study was used to compare the crocin production between conventional plantation and synthetic biology approach. A study showed the decrement of year wise saffron plantation, which could be caused by soil nutrient reduction that was not related to the water resource availability (1). Even though the saffron production is quite fluctuating until 2008, the plantation area was decreased significantly. The research also found that there is a declining trend in one of the largest producer, Kashmir, due to urbanization. In order to obtain the crocin with high purity, the process of compound extraction also needed. Currently, the synthetic production of crocin is still unknown. Regardless, there is a potential for producing crocin through synthetic biology. Thus, iGEM Uppsala 2017 is trying to cut off the saffron plantation process for producing crocin. Instead, the crocin production will be replaced in *E. coli*. Expectantly, this will diminish the extensive of land use for cultivation and reduce unsubstantial residue production. To compare between the production of crocin in the traditional plantation and by using synthetic biology as the tools, this market analysis was conducted.

Before getting the actual comparison, the analysis of the market analysis is based on the whole production of crocin from traditional saffron plantation until the crocin extraction with conventional method. Comparably, we did the analysis of the 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

Shown in the Table B, a freshly picked flower generates an average of 30 mg of fresh saffron or 7 mg when if it is dried, to get one gram of dry saffron it takes about 150 flowers where a kilogram of flowers can produce 12 g of dried saffron where 1 kg of dry saffron requires 110,000-170,000 flowers (5). Based on the number, the production of crocin can be linearly calculated with 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 degrade naturally in the stigmas cells when saffron is in the phase of drying, storage to extraction. According to Straubinger *et al.* (2), the crocin compounds can be found from the stigma after the natural degradation which involve 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 generates 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 to the 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 huge sources which is needed, but also many human resources will be required. Even the biggest producer of saffron (Iran) can 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 has the value nearly US$ 620 Mn (7). Nevertheless, the production of crocin may have an obstacle if it is produced in the conventional way (plantation) or in another word, the production may cost much more expensive to extract crocin inspite of using or selling it as a saffron.

iGEM Uppsala 2017 is trying to use synthetic biology to produce crocin. By constructing three different enzymes which can be used to convert the zeaxanthin into crocin. If the enzyme can be produced and required to overcome the problem of mass production of the crocin and the production could be much cheaper. Changing the production from plantation 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 place for plantation, human resources, instrumentation, insulation and buildings, and some other facility which needed. In the market, 1 gram of crocin can be bought 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 plantation of saffron.

The benefit of using synthetic biology in producing compound may face some problems including the worldwide perspective of its product. Here, we tried to identify the existing market within similar product (enzymes form big company).

Table D. The future problem and potential 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 plantation
Socio-cultural	Technological
● GMO opinion will rise again ● Available job or decreasing the job (for farmer) → this job prevents rural migration ● Urbanisation put stress on the expansion of saffron plantation	● More invention in bio-product related, packaging, protein purification, and etc. ● More in the microbe production technology

Environmental	Legal
● Reduce the land use, water and related to the plantation ● 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 give 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

<table>
<tr><td colspan="3">Threat of new entry
1. Several researcher also are conducting the same aim with different enzymes. So, there could be someone which is doing the similar stuff.
2. Proper plan with mass scale of enzyme production might be harder.</td></tr>
<tr><td>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.</td><td>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 existed company may also start producing the similar enzymes.</td><td>Bargaining power of customers
1. Because the production cost will be cheaper, the cost for selling the crocin may be even cheaper than existed crocin in the market. Therefore, the market will get attracted more</td></tr>
<tr><td colspan="3">Threat of substitutes
1. There are several potential enzymes from different pathway 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 be chemically synthesized</td></tr>
</table>

If the crocin production from synthetic biology can be produced, there are several aspect which may support the sustainable development perspective. The water consumption of conventional plantation 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 plantation which can be used for other purposes or focusing on the utilization of saffron.

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